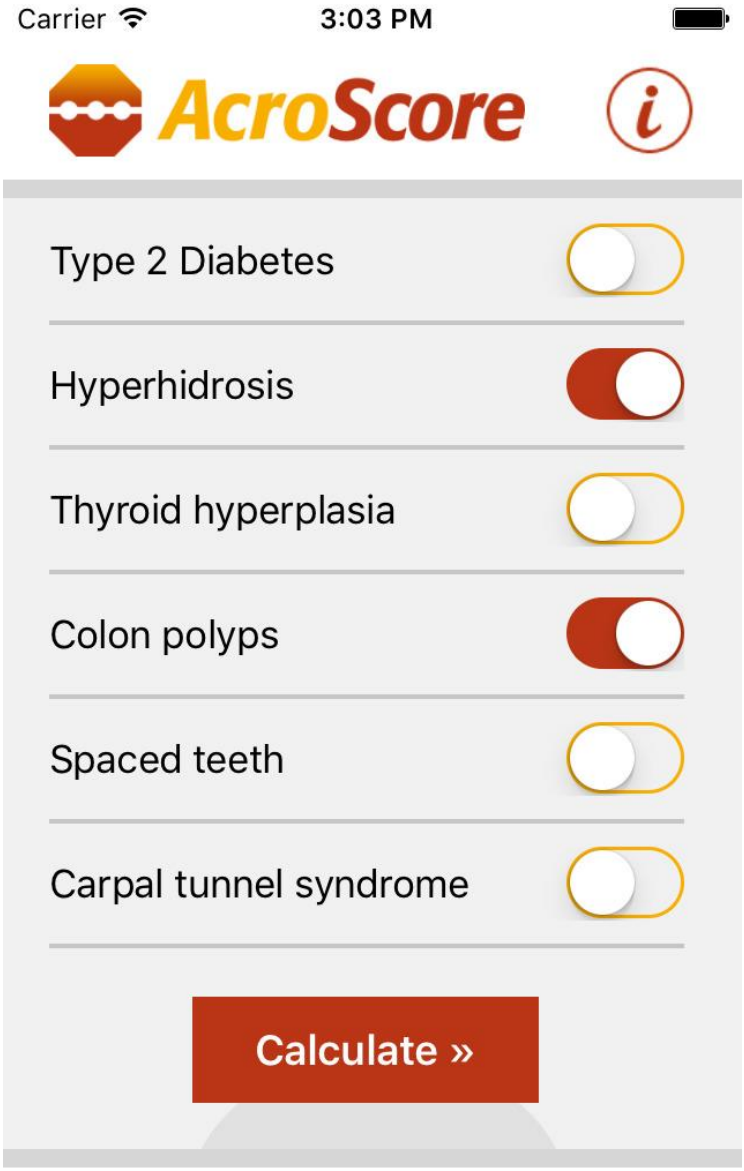
Clinically Applied Endocrinolgy Algorithms

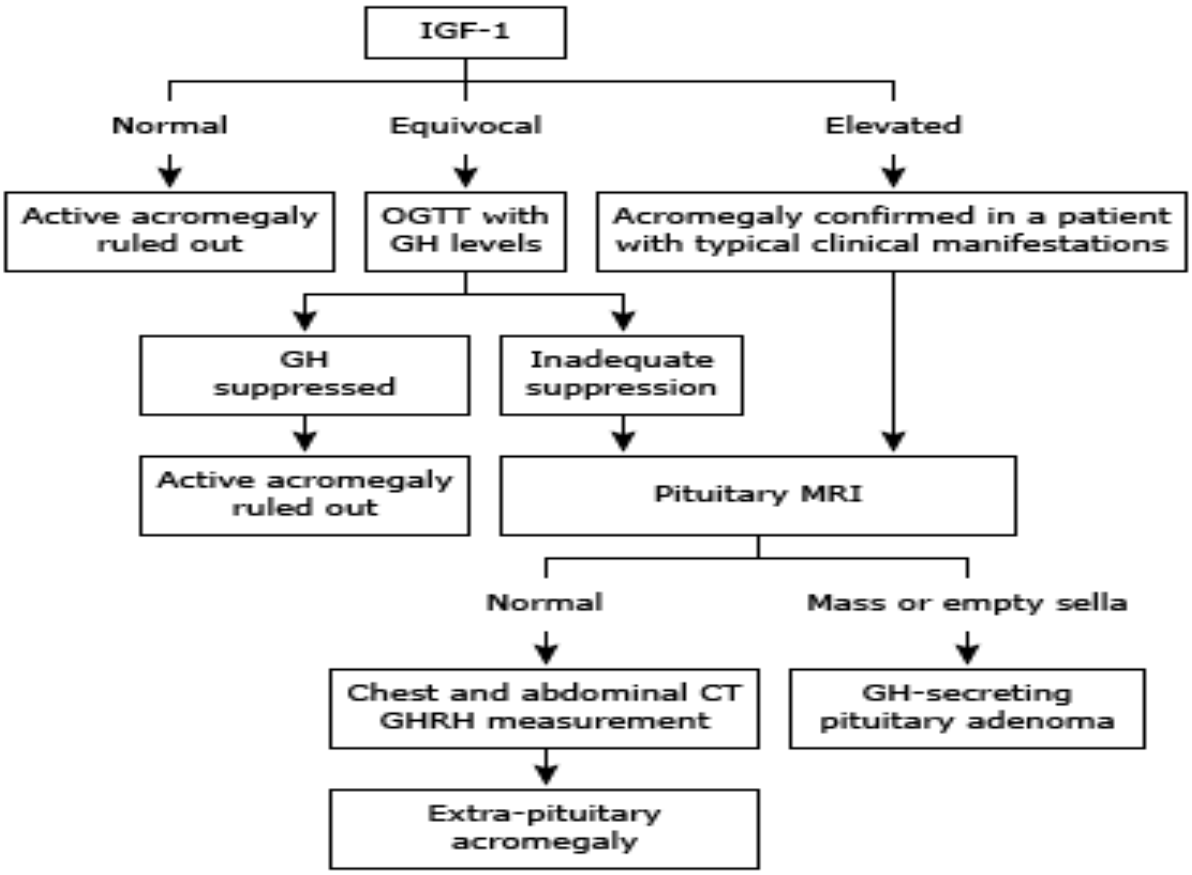
Pituitary disorders; Management of acromegaly

ACRO score: a 14-point scoring system developed. A score of 0 excludes the risk of acromegaly , scores 1-5 comprise a grey area; scores >5 indicate that a diagnosis of acromegaly cannot be excluded



Skeletal changes are irreversible in Acromegaly, so Early diagnosis Help to identify the tumor early And ease the surgical intervention

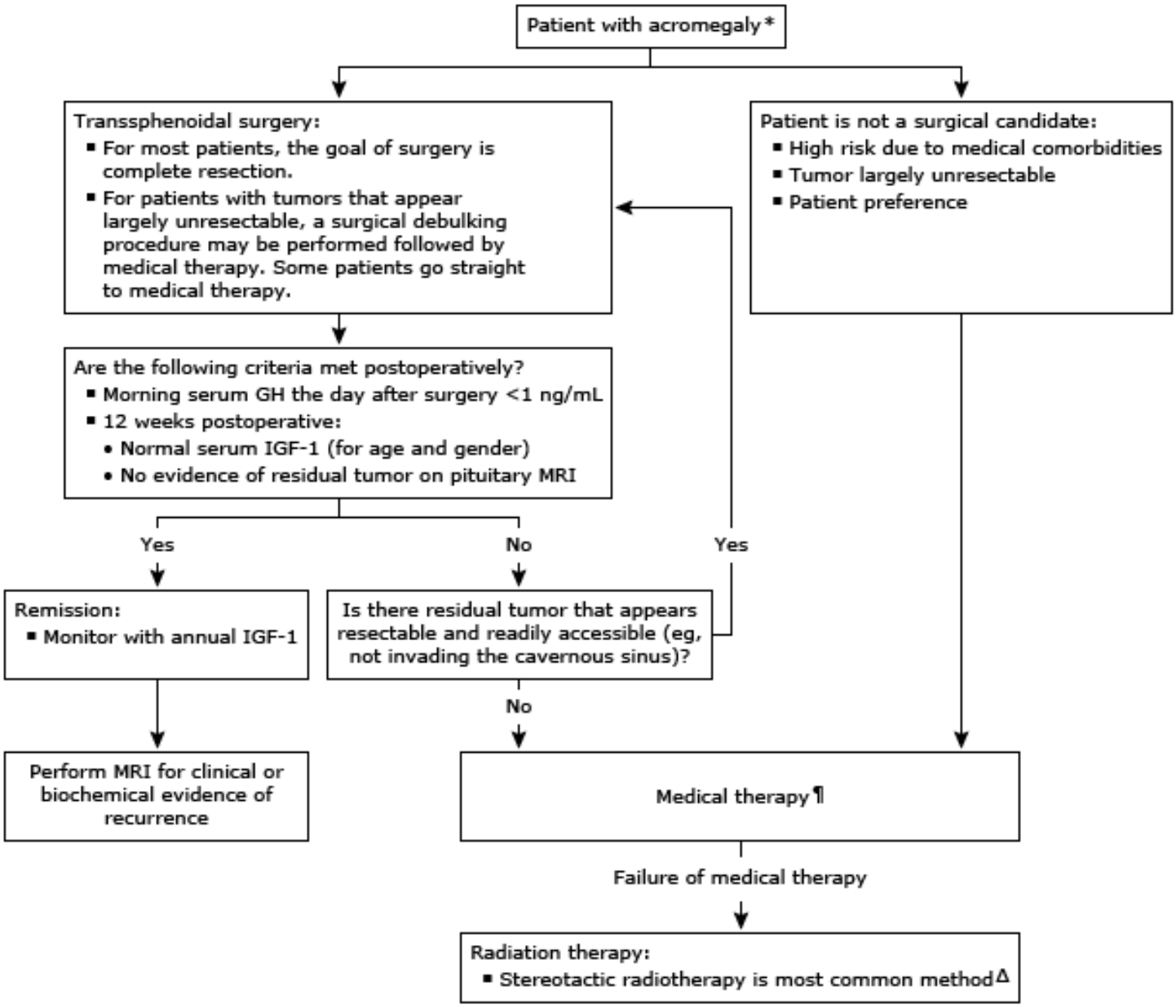
Pituitary disorders; Management of acromegaly



Endocrine society of Endocrinology 2022

- The most specific dynamic test for establishing the diagnosis of acromegaly is an OGTT.
- **OGTT** is ***the gold standard for determining control of GH secretion after surgical treatment***, but it does not appear to be useful in assessing biochemical control in patients receiving medical therapy with somatostatin analogs
- The increase in serum IGF-1 is often disproportionately greater than that in GH for two reasons: GH secretion fluctuates more, and GH stimulates the secretion of IGF-1- binding protein-3 (IGFBP-3), the major IGF-1 binding protein in serum.
- In normal subjects, serum IGF-1 concentrations are highest during puberty and decline gradually thereafter.
- Values are significantly lower in adults over the age of 60 years than in younger subjects. Thus, an apparently "normal" value in a patient aged 70 years may in fact be elevated.
- conditions that are associated with lower serum IGF-1 concentrations including Hypothyroidism , Malnutrition, poorly controlled type 1 diabetes ,liver failure, renal failure & oral estrogen use

Pituitary disorders; Management of acromegaly


Patient with acromegaly*
Transsphenoidal surgery:
For most patients, the goal of surgery is complete resection.
For patients with tumors that appear largely unresectable, a surgical debulking procedure may be performed followed by medical therapy. Some patients go straight to medical therapy.
Patient is not a surgical candidate:
High risk due to medical comorbidities
Tumor largely unresectable
Patient preference
Are the following criteria met postoperatively?
Morning serum GH the day after surgery <1 ng/mL
12 weeks postoperative:
Normal serum IGF-1 (for age and gender)
No evidence of residual tumor on pituitary MRI
Yes
No
Yes
Remission:
Monitor with annual IGF-1
Is there residual tumor that appears resectable and readily accessible (eg, not invading the cavernous sinus)?
No
Perform MRI for clinical or biochemical evidence of recurrence
Medical therapy¶
Failure of medical therapy
Radiation therapy:
Stereotactic radiotherapy is most common method∆

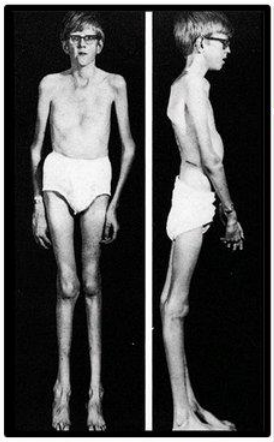
- Follow up for possibility of Recurrence is important and should be done on yearly basis (IGF , GH level , visual field and MRI sella) as ~**2–8%** of patients who achieve remission with surgery will experience disease recurrence within 5 years
- Intra individual biological variability, assay imprecision and physiological factors are known contributors to falsely elevated IGF-1, dopamine agonist therapy and CKD should also be considered.
- Ectopic acromegaly is almost always secondary to an NET originating in the lung and pancreas .Association of pheochromocytoma may present

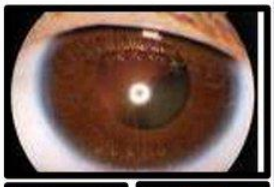
Touraine–Solente–Gole syndrome also known as Pachydermoperiostitis(PDP) is defined by –

- the presence of digital clubbing,
- pachyderma (thickening of the skin), and
- periostosis (swelling of periarticular tissue and subperiosteal new bone formation)

- It is a familial disorder inherited as an autosomal dominan trait with variable expression.
- PDP is a rare genetic disease.[1]At least 204 cases of PDP have been reported.[1]
- The precise incidence and prevalence of PDP are still unknown.[1] A prevalence of 0.16% was suggested by Jajic[2].

Figure 6: Pre- and post-operative photographs, 4 weeks after frontal





24) Marfan Syndrome

Clinical features

Major criteria:

- ✓ Ectopia lentis.
- ✓ Aortic dilatation or dissection.
- ✓ Family history

Systematic score features :

Wrist AND thumb sign	3
Wrist OR thumb sign	1
Pectus carinatum deformity	2
Pectus excavatum or chest asymmetry	1
Hindfoot deformity	2
Pes planus	1
Pneumothorax	2
Dural ectasia	2
Protrusio acetabuli	2
Reduced upper segment/lower segment ratio AND increased arm/height ratio AND no severe scoliosis	1
Scoliosis or thoracolumbar kyphosis	1
Reduced elbow extension	1
Facial features (3/5): dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia	1
Skin striae	1
Myopia >3 diopters	1
Mitral valve prolapse	1

❖ **Mode of inheritance?**

- ✓ Autosomal dominant
- ✓ FBN1 gene

❖ **Monitoring?**

- ✓ Annual echocardiogram.

How to confirm the diagnosis?

Ghent criteria

- 2 major criteria
- 1 major + FBN1 gene mutation
- 1 major + ≥7 more systematic score

Pediatric On Squares
@OnSquares

❖ **Most common cardiac defect ?**

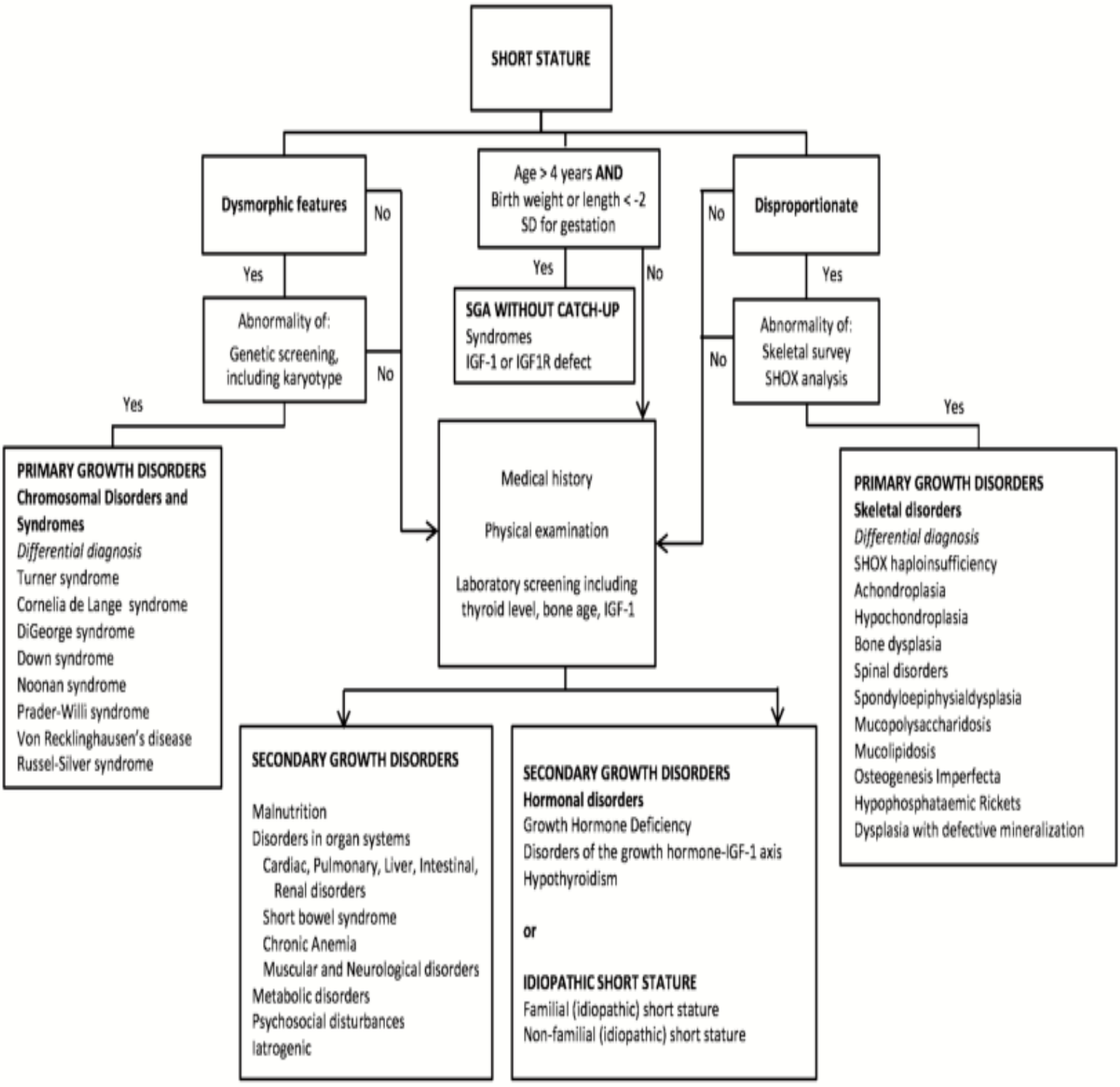
- ✓ **Mitral valve prolapse**
- ✓ Aortic root dilatation

❖ **Most common cause of death?**

- ✓ Cardiovascular complications
- ✓ Rupture aortic root dilatation

- been reported in some patients

Pituitary disorders; Management of short stature



A child is considered short if: His height is less than 3rd percentile or 2 standard deviations below the mean height for that age. Even if the height is within normal percentiles but growth velocity is consistently below 25th percentile over 6-12 months of observation.

➢ Pituitary disorders; Management of short stature

Short Stature

ormal Variants (<2SD)
- Familial Short Stature
- Constitutional Growth Delay

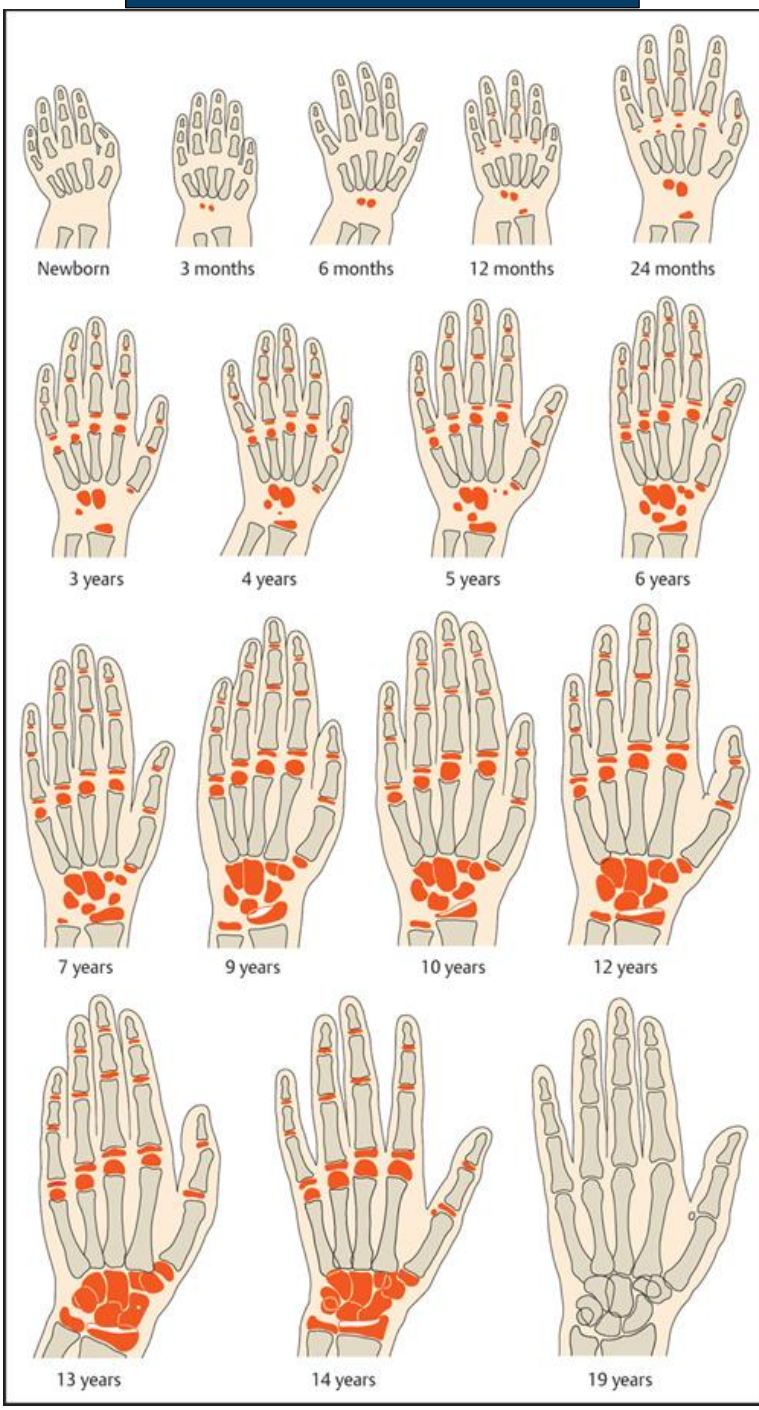
Pathologic (<3SD)

Proportionate

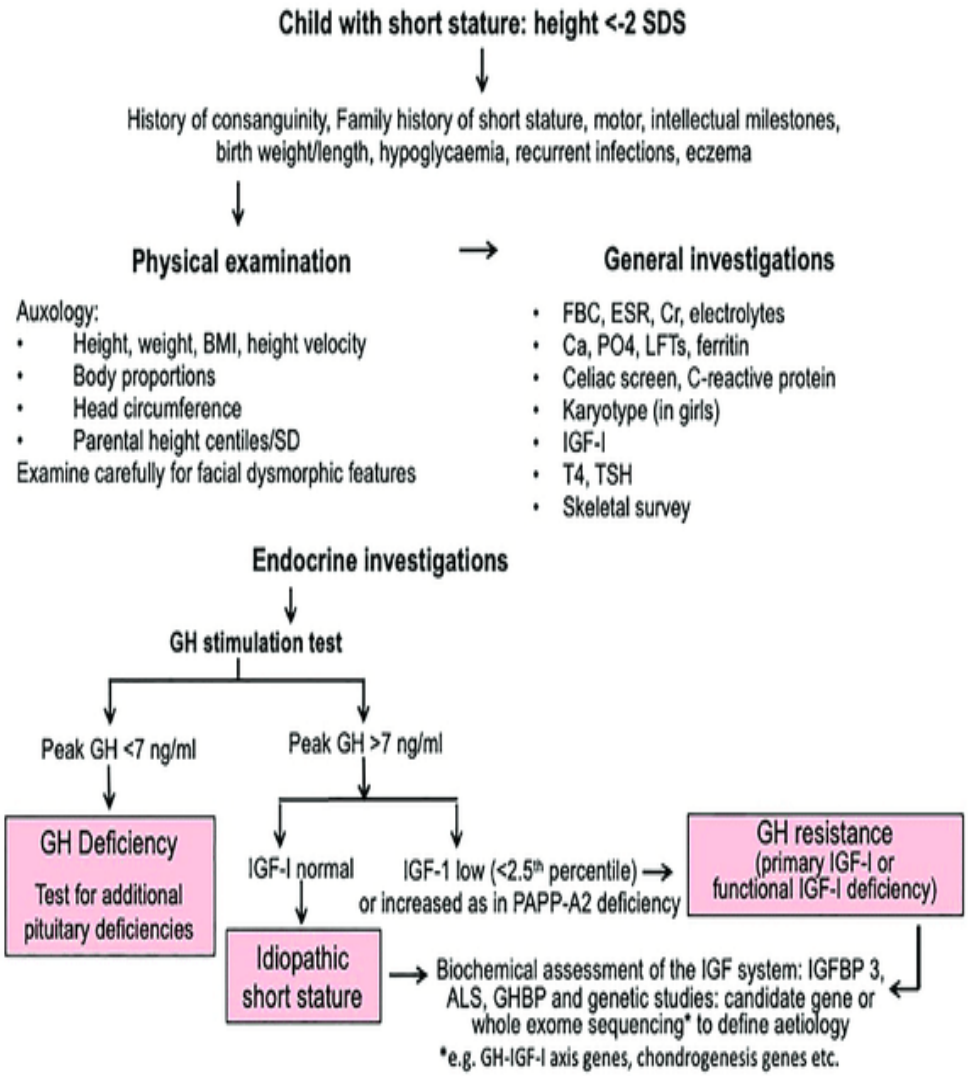
1. **Systemic diseases**
   - Chronic Anemia
   - Chronic renal failure
   - Renal tubular acidosis
   - Chronic Asthma
   - Congenital heart disease
   - Chronic infections
   - Malabsorption
   - Chronic liver disease.
2. **Malnutrition**
3. **Endocrine disorders**
   - Growth hormone deficiency
   - Hypothyroidism
   - Cushing syndrome
   - Diabetes mellitus
   - Diabetes insipidus (due to tumors, neonatal insult)
   - Hypopitutarism
   - Hypogonadism.
4. **Intrauterine growth retardation (IUGR)**
5. **Genetic syndromes – common examples:**
   - Turner's syndrome
   - Noonan's syndrome
   - Russel Silver syndrome
   - Seckel's syndrome
   - Down's syndrome
6. **Inborn error of metabolism**
7. **Psychosocial dwarfism**
8. **Idiopathic Short Stature**

Disproportionate
- Skeletal dysplasias
- Rickets

Bone Age assessment in x ray wrist



Pituitary disorders; Management of short stature


Child with short stature: height <-2 SDS
History of consanguinity, Family history of short stature, motor, intellectual milestones, birth weight/length, hypoglycaemia, recurrent infections, eczema
Physical examination
Auxology:
Height, weight, BMI, height velocity
Body proportions
Head circumference
Parental height centiles/SD
Examine carefully for facial dysmorphic features
General investigations
FBC, ESR, Cr, electrolytes
Ca, PO4, LFTs, ferritin
Celiac screen, C-reactive protein
Karyotype (in girls)
IGF-I
T4, TSH
Skeletal survey
Endocrine investigations
GH stimulation test
Peak GH <7 ng/ml
Peak GH >7 ng/ml
GH Deficiency
Test for additional pituitary deficiencies
IGF-I normal
IGF-1 low (<2.5th percentile) or increased as in PAPP-A2 deficiency
GH resistance (primary IGF-I or functional IGF-I deficiency)
Idiopathic short stature
Biochemical assessment of the IGF system: IGFBP 3, ALS, GHBP and genetic studies: candidate gene or whole exome sequencing* to define aetiology
*e.g. GH-IGF-I axis genes, chondrogenesis genes etc.

Somatropin >>> Growth hormone

Somatomedin c >>> IGF 1

Sandostatin >>> octreotide

Somatostatin >>> Growth hormone inhibiting hormone

How To Differentiate

	Constitutional delay	Familial short stature	Growth hormone deficiency
Growth curve	Growth velocity along or parallel to the lower percentiles of the growth curve	Growth velocity is parallel to but below the normal growth curve	Height or length > 3 SD below the mean
Family history	Positive late bloomers	One or two parents are short	Depends on the cause
Bone age	Mildly delayed	Equal to chronological age	Delayed
Hormonal studies	Normal	Normal	Low IGF-1 and low IGFBP-3
Treatment	Reassurance Some may benefit from testosterone short course if puberty is delayed	Reassurance and monitoring	Growth hormone

IGF-1 insulin-like growth factor 1, *IGFBP-3* IGF binding protein 3

Prader-Willi
Board Highlights
Genetics

- ✓ Majority: 15q11-q13 paternal chromosome deletion
  - Minority: maternal uniparental disomy
- ✓ Genomic imprinting: parent-specific gene expression
  - Angelman syndrome: 15q maternal chrom. deletion

Select Physical Characteristics

- Small hands *& tapered fingers*

- Small feet

- Severe obesity

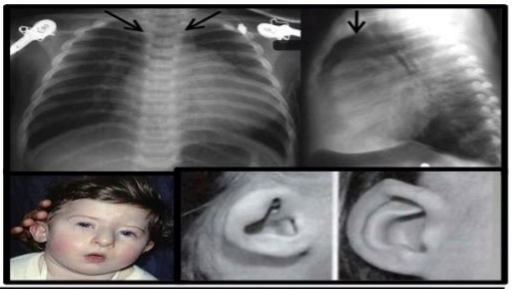
- Almond-shaped eye

Almond-shaped eyes are commonly found in Prader Willi syndrome.

Round-shaped eye is shown below for comparison

Round-shaped eye

13) DiGeorge syndrome (Velocardiofacial syndrome)



Clinical features (CATCH 22)

- ✓ Cardiac defect
- ✓ Abnormal face (Hooded eyelids, ptosis, hypoplasia of auricles)
- ✓ Thymic hypoplasia (T cell abnormalities)
- ✓ Cleft palate
- ✓ Parathyroid aplasia / hypoplasia
- ✓ Hypernasal speech (Velopharyngeal incompetence)
- ✓ Hypotonia in infancy
- ✓ Learning disabilities & behavioral problems

@OnSquares

❖ **Other names ?**
- ✓ 22q11.2 deletion syndrom
- ✓ Shprintzen syndrome

❖ **Common cardiac defect?**
- ✓ Interrupted aortic arch
- ✓ Truncus arteriosus
- ✓ Tetralogy of Fallot
- ✓ VSD

❖ **Laboratory finding ?**
- ✓ Hypocalcemia
- ✓ Low PTH
- ✓ Low IgG

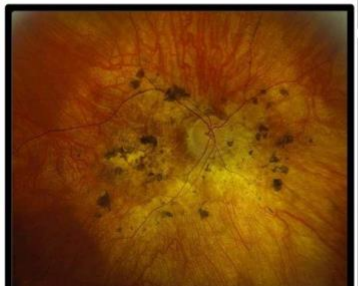
Pediatric On Squares

❖ **Mode of inheritance?**
- ✓ Autosomal dominant

❖ **It is the MOST COMMON :**
- ✓ Microdeletion syndrome
- ✓ T-Cell disorder

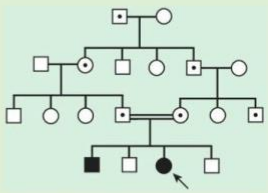
❖ **Which vaccine should be avoided ?**
- ✓ live attenuated vaccine if immunodeficient

17) Bardet–Biedl syndrome (Laurence-Moon-Biedl syndrome)



❖ **Clinical features**
- ✓ Obesity
- ✓ Postaxial polydactyly
- ✓ Hypogonadism
- ✓ Retinitis pigmentosa
- ✓ Rod-cone dystrophy
- ✓ Mental retardation
- ✓ Polyuria and polydipsia
- ✓ Renal anomalies

❖ **Mode of inheritance?**
- ✓ Autosomal recessive



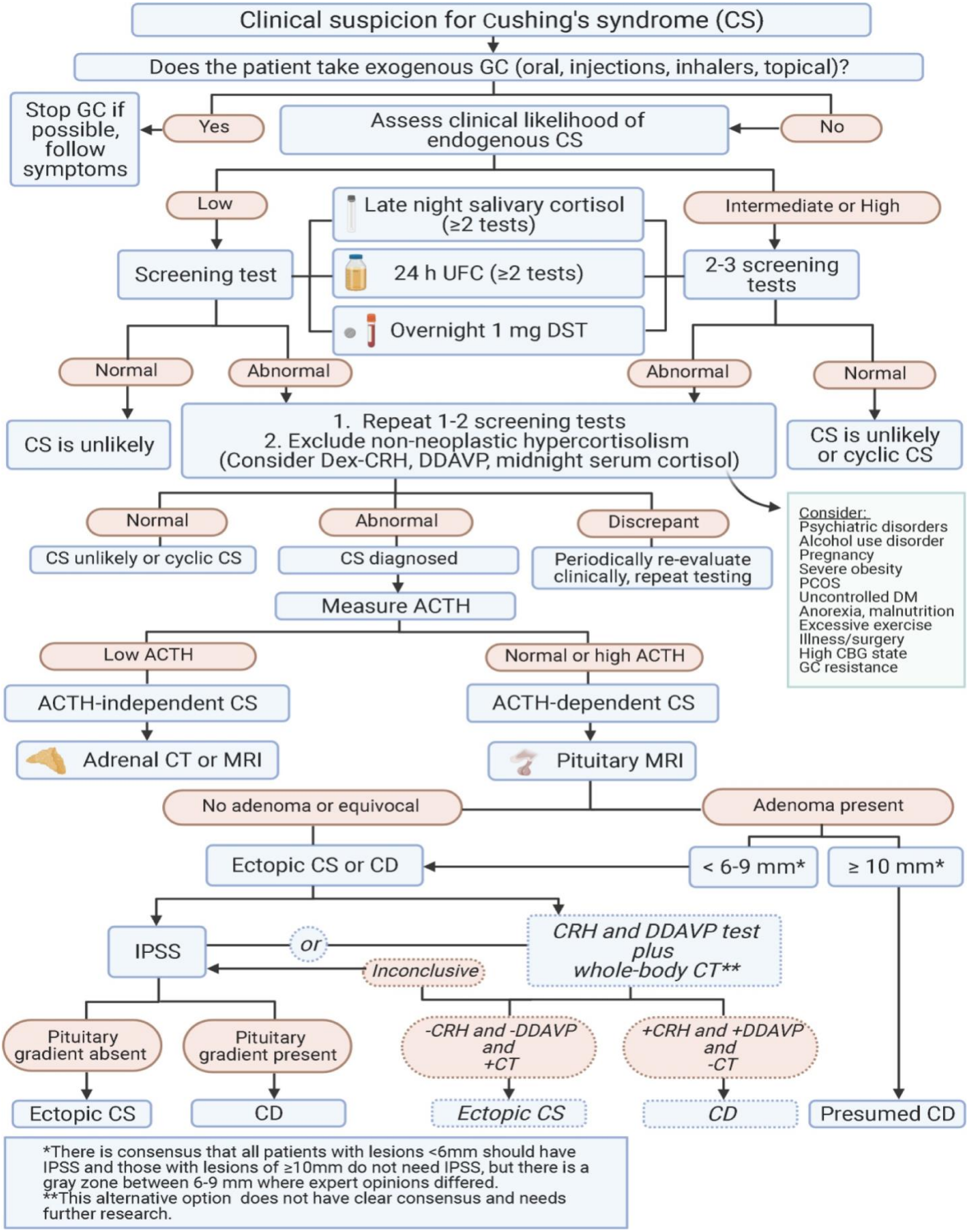
❖ **Most common gastrointestinal association?**
- ✓ Hirschsprung disease

Pediatric On Squares

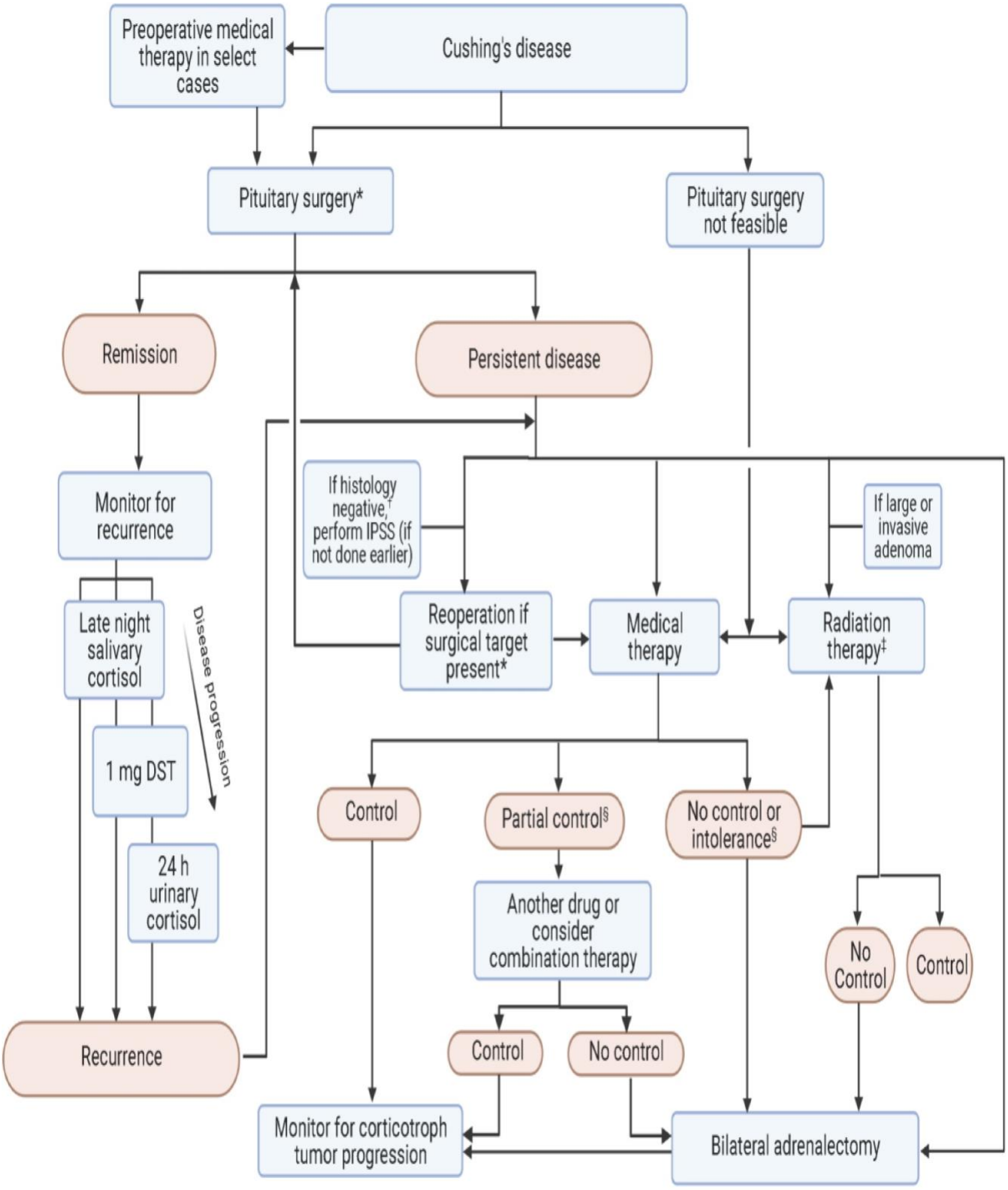
❖ **What is the cause of polyuria and polydipsia?**
- ✓ Nephrogenic diabetes insipidus

@OnSquares

Pituitary disorders; Management of Cushing's disease



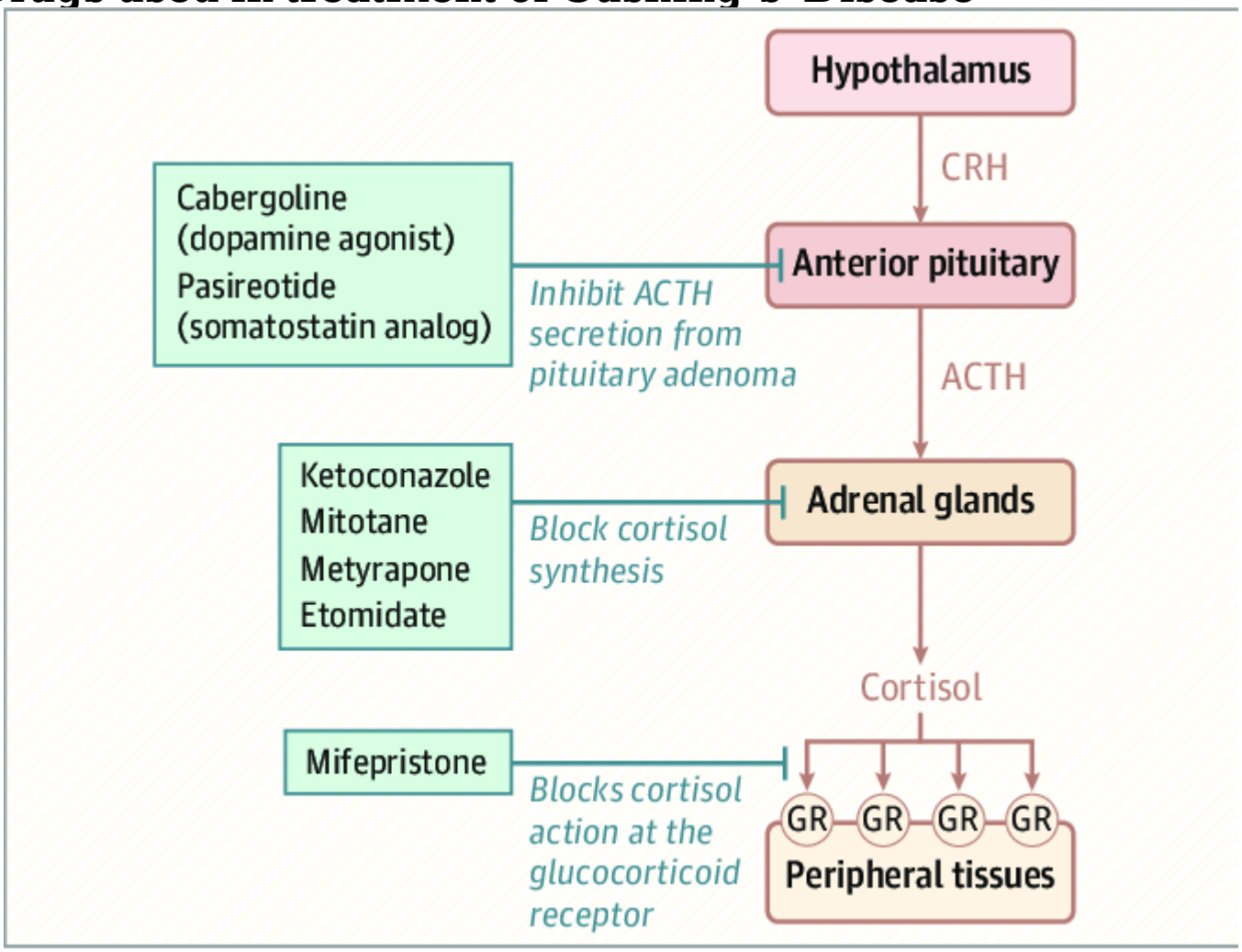
Pituitary disorders; Management of Cushing's disease

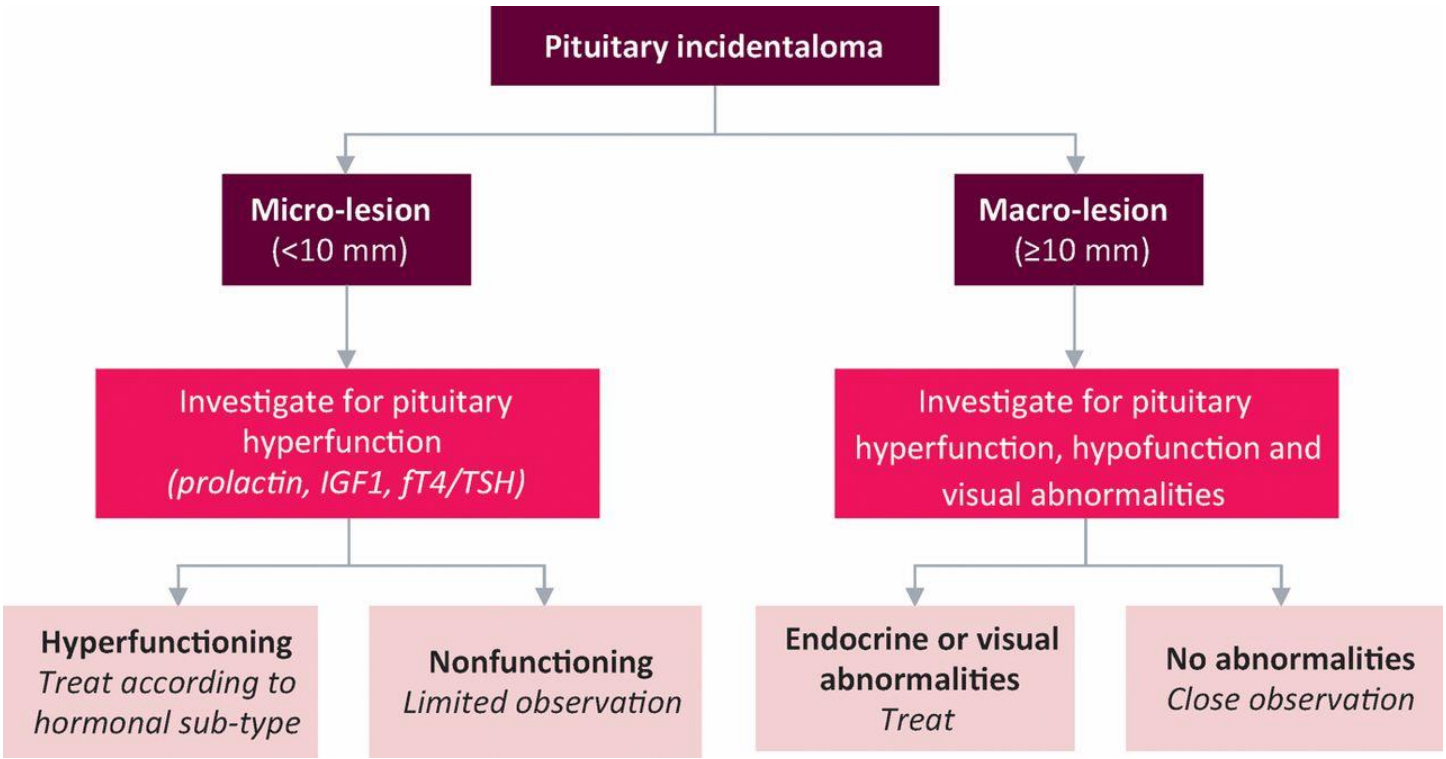


*Pituitary surgery should be performed by an experienced surgeon;
†Absence of ACTH-staining adenoma;
‡Lifelong monitoring for hypopituitarism and secondary neoplasia in the radiation field required.
§On maximum tolerated dose of the drug

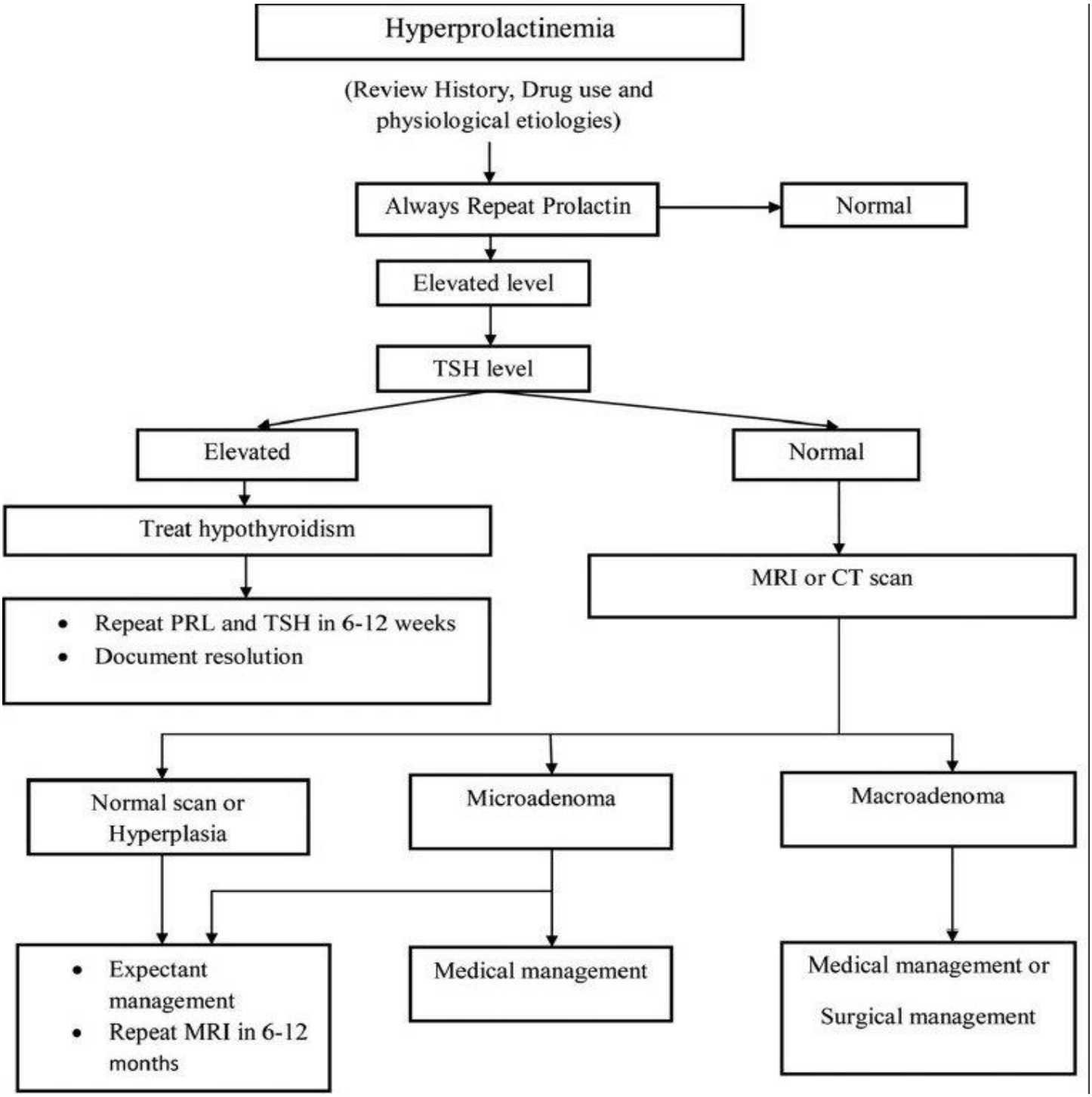
Pituitary disorders; Management of Cushing's disease

Drugs used in treatment of Cushing's Disease



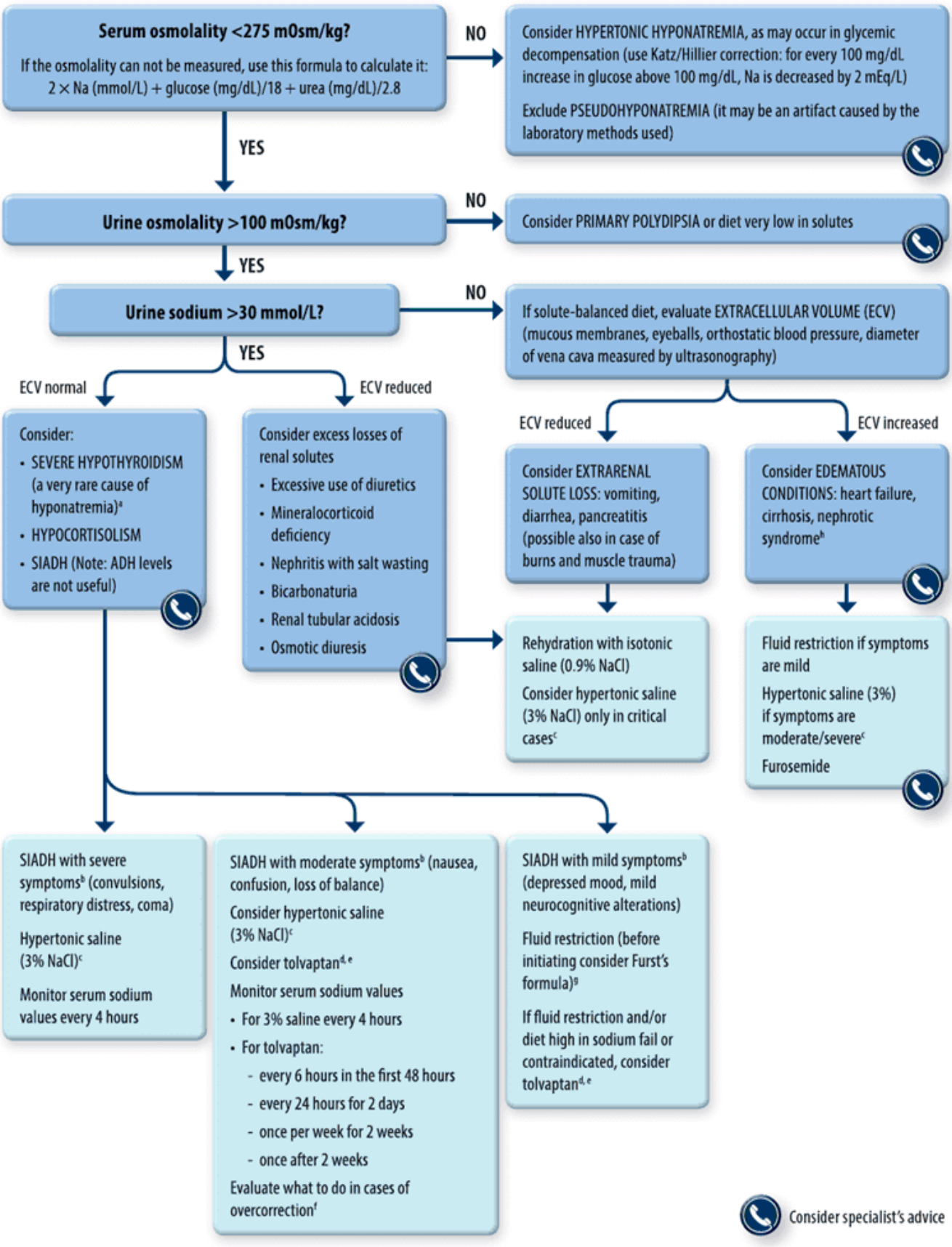


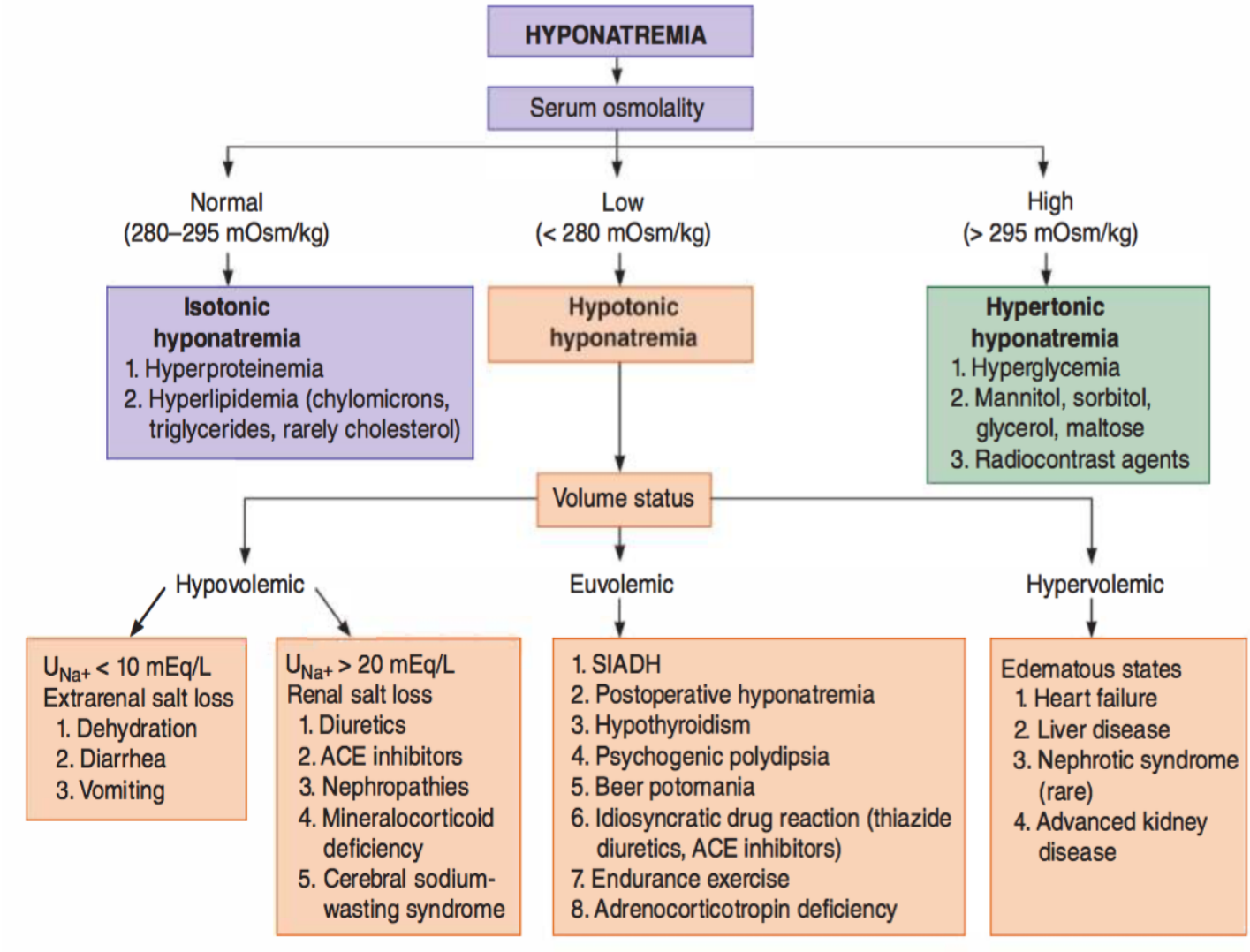
Pituitary disorders; Management of hyperprolactinemia



- Always consider to exclude **pregnancy, PCOS, drugs (GIT, antidepressants and antipsychotics) and chest wall disorders** in dealing with hyperprolactinemia

Pituitary disorders: SIADH (Hyponatremia management)


Serum osmolality <275 mOsm/kg?
If the osmolality can not be measured, use this formula to calculate it: 2 × Na (mmol/L) + glucose (mg/dL)/18 + urea (mg/dL)/2.8
NO
Consider HYPERTONIC HYPONATREMIA, as may occur in glycemic decompensation (use Katz/Hillier correction: for every 100 mg/dL increase in glucose above 100 mg/dL, Na is decreased by 2 mEq/L)
Exclude PSEUDOHYPONATREMIA (it may be an artifact caused by the laboratory methods used)
YES
Urine osmolality >100 mOsm/kg?
NO
Consider PRIMARY POLYDIPSIA or diet very low in solutes
YES
Urine sodium >30 mmol/L?
NO
If solute-balanced diet, evaluate EXTRACELLULAR VOLUME (ECV) (mucous membranes, eyeballs, orthostatic blood pressure, diameter of vena cava measured by ultrasonography)
YES
ECV normal
ECV reduced
Consider:
• SEVERE HYPOTHYROIDISM (a very rare cause of hyponatremia)a
• HYPOCORTISOLISM
• SIADH (Note: ADH levels are not useful)
Consider excess losses of renal solutes
• Excessive use of diuretics
• Mineralocorticoid deficiency
• Nephritis with salt wasting
• Bicarbonaturia
• Renal tubular acidosis
• Osmotic diuresis
ECV reduced
ECV increased
Consider EXTRARENAL SOLUTE LOSS: vomiting, diarrhea, pancreatitis (possible also in case of burns and muscle trauma)
Consider EDEMATOUS CONDITIONS: heart failure, cirrhosis, nephrotic syndromeb
Rehydration with isotonic saline (0.9% NaCl)
Consider hypertonic saline (3% NaCl) only in critical cases[c]
Fluid restriction if symptoms are mild
Hypertonic saline (3%) if symptoms are moderate/severe[c]
Furosemide
SIADH with severe symptomsb (convulsions, respiratory distress, coma)
Hypertonic saline (3% NaCl)[c]
Monitor serum sodium values every 4 hours
SIADH with moderate symptomsb (nausea, confusion, loss of balance)
Consider hypertonic saline (3% NaCl)[c]
Consider tolvaptan[d,e]
Monitor serum sodium values
• For 3% saline every 4 hours
• For tolvaptan:
- every 6 hours in the first 48 hours
- every 24 hours for 2 days
- once per week for 2 weeks
- once after 2 weeks
Evaluate what to do in cases of overcorrection[f]
SIADH with mild symptomsb (depressed mood, mild neurocognitive alterations)
Fluid restriction (before initiating consider Furst's formula)g
If fluid restriction and/or diet high in sodium fail or contraindicated, consider tolvaptan[d,e]
Consider specialist's advice



Treatment of Severe Symptomatic Hyponatremia

Serum sodium < 125 mEq per L with severe symptoms (e.g., seizures, mental status changes)

Infuse 3% saline (1 to 2 mL per kg per hour) with goal of increasing serum sodium level by 6 to 8 mEq per L (not to exceed 10 to 12 mEq per L in the first 24 hours or 18 mEq per L in 48 hours)

Consider desmopressin, 1 to 2 mcg every four to six hours

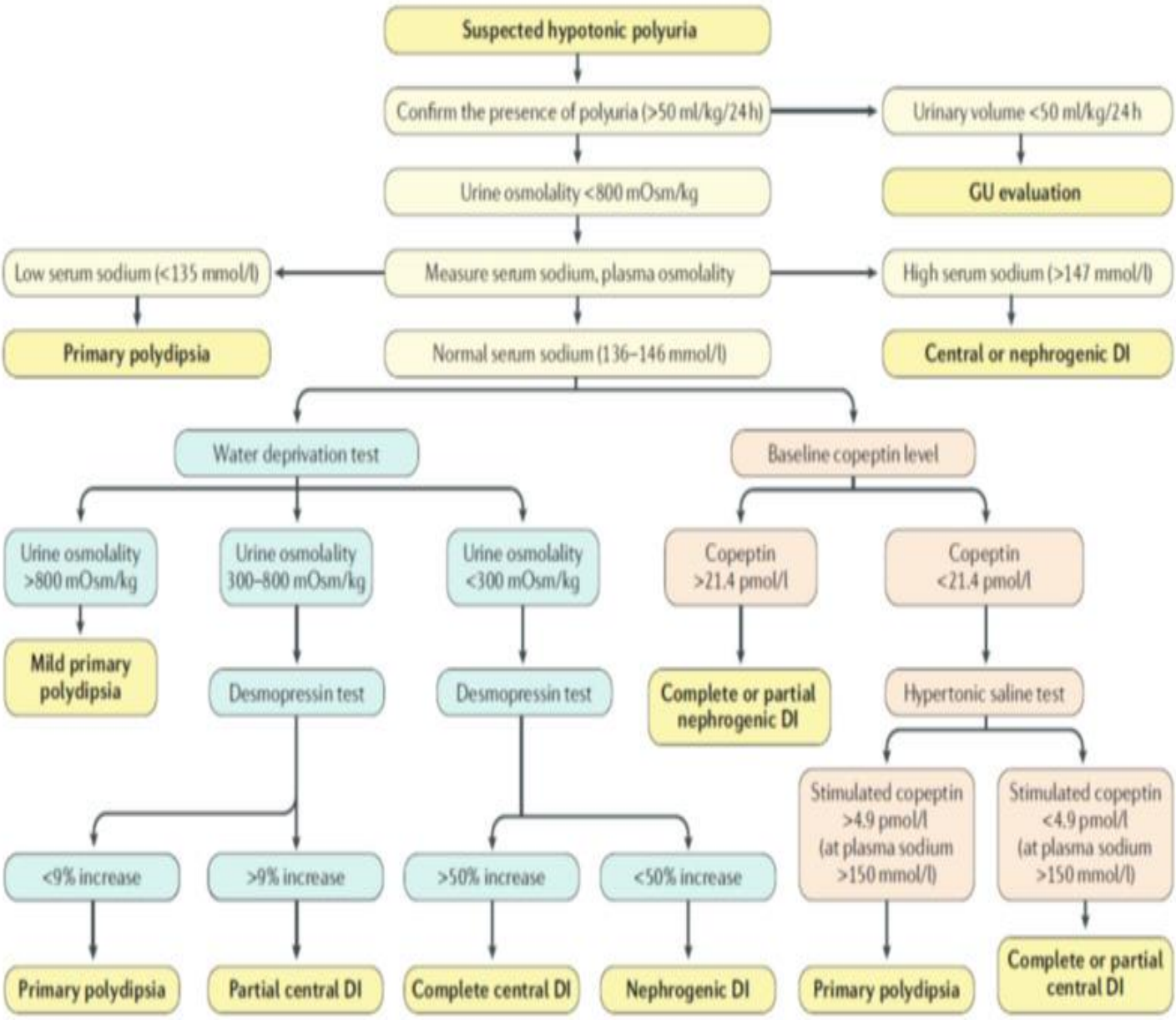
Give single intravenous bolus of 100 to 150 mL 3% saline with goal of increasing serum sodium level by 2 to 3 mEq per L; check sodium level every 20 minutes until symptoms resolve; may repeat bolus twice if symptoms do not resolve

Symptom resolution

Check serum sodium level every two hours; adjust infusion rate and switch to isotonic saline

Determine underlying cause (see Table 1)

Pituitary disorders: DI (Diabetes insipidus management)



DI is a busy man disease , water intake prevents deterioration

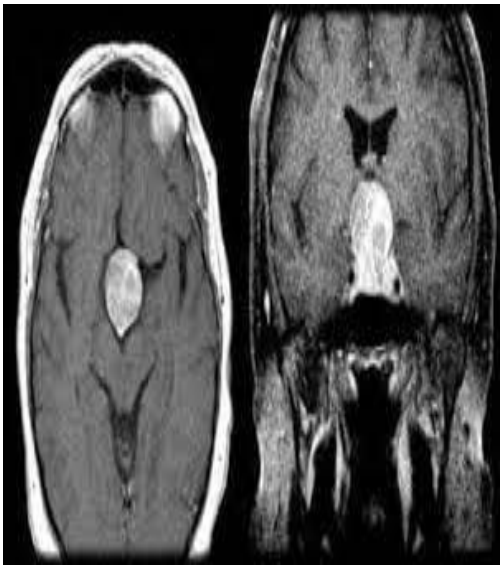
Serum osmolarity Equation

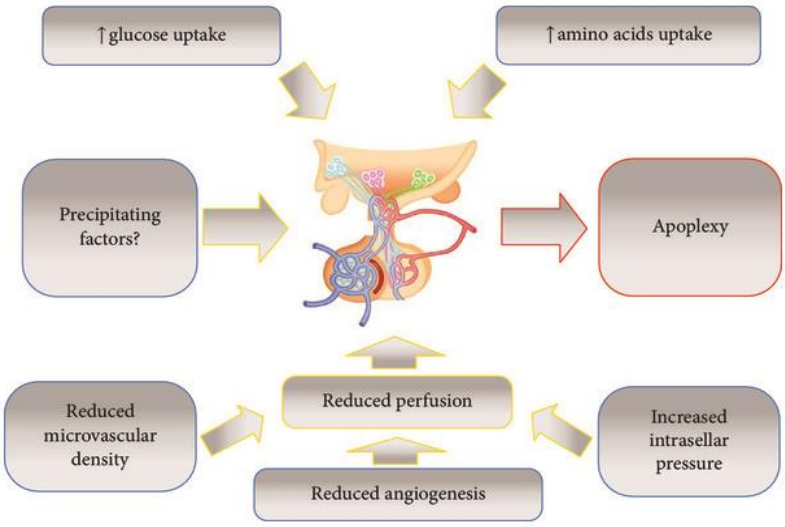
$$2Na\ (mEq/L) + 2K\ (mEq/L) + \frac{glucose\ (mg/dL)}{18} + \frac{BUN\ (mg/dL)}{2.8}$$

that is,

$$2(Na + K) + \frac{BUN}{2.8} + \frac{glucose}{18}$$

Pituitary disorders; Management of pituitary apoplexy





Remember > STEROIDS replacement is the most important at time of presentation

Suspected pituitary apoplexy

- Supportive measures to ensure haemodynamic stability
- Assessment and management of fluid/electrolyte balance
- Consider hydrocortisone replacement

- Urgent biochemical and endocrine assessment (full blood count, urea and electrolytes, liver function tests clotting screen, IGF1, GH, PRL, TSH, T4, LH, FSH, cortisol, testosterone or oestradiol)

- Urgent MRI to confirm diagnosis
  or
- A dedicated pituitary CT scan if MRI is contraindicated

- Liaise with regional endocrine and neurosurgical team immediately after the diagnosis is confirmed

- Severely reduced visual acuity
- Severe and persistent or deteriorating visual field defects
- Deteriorating level of consciousness

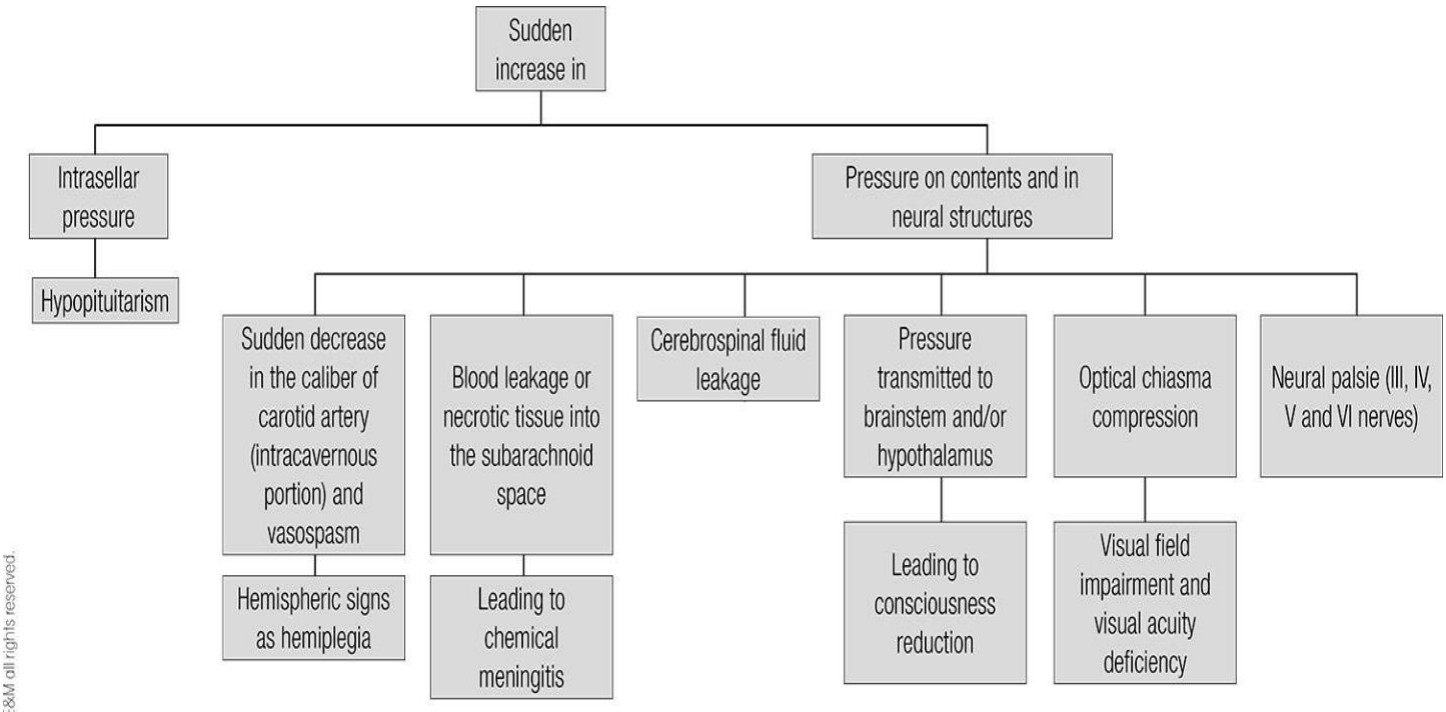
Yes → Consider surgical management

No → Conservative management
Close monitoring (neurological, visual and endocrine)

Patient stable or improving

Yes → Continue conservative management

No → Consider surgical management


Sudden increase in
Intrasellar pressure
Hypopituitarism
Pressure on contents and in neural structures
Sudden decrease in the caliber of carotid artery (intracavernous portion) and vasospasm
Hemispheric signs as hemiplegia
Blood leakage or necrotic tissue into the subarachnoid space
Leading to chemical meningitis
Cerebrospinal fluid leakage
Pressure transmitted to brainstem and/or hypothalamus
Leading to consciousness reduction
Optical chiasma compression
Visual field impairment and visual acuity deficiency
Neural palsie (III, IV, V and VI nerves)

AE&M all rights reserved.

Clinical presentation
Sudden onset headache
Vomiting, nausea
Photophobia
Meningism
Visual field and acuity defects
Diplopia/opthalmoplegia
Pyrexia
Cranial nerve palsy
Third nerve (more frequent)
Fourth nerve (trochlear)
Fifth nerve (1st and 2nd branches of trigeminal)
Sixth nerve (abducens)
Altered mental status
Seizure
Reduced conscious level
Facial pain/impaired facial sensation
Collapse
Hemiparesis
Sudden Death

Endocrine defect
Hypopituitarism
Panhypopituitarism
ACTH deficiency
Central Hypothyroidism
Hypogonadism
Growth hormone deficiency
Diabetes insipidus
Hyponatremia

Pituitary disorders; Management of Sheehan syndrome

Sheehan's Syndrome

Sheehan's syndrome results from infarction of pituitary gland during post-partum period.

Post-partum pituitary infarction occurs because of the enlarged pituitary gland of pregnancy is more vulnerable to ischemia of post-partum hemorrhage and systemic hypotension.

It can present with failure to establish lactation after birth, amenorrhoea or other features of hypopituitarism.

Clinical features:

Lactation failure (earliest sign)
Secondary Amenorrhea
Hypogonadism
Asthenia and weakness
Loss of hair
Hypopigmentation
Diabetes insipidus
Empty Sella in MRI report

Source & Image : Researchgate.net

Treatment is to replace deficit hormones

TREATMENT

Hormone replacement

- Hydrocortisone or prednisolone is replaced first because thyroxine therapy can exacerbate glucocorticoid deficiency and theoretically induce an adrenal crisis.
- thyroxine replacement
- gonadotropin replacement
- Replacement of growth hormone is necessary in children with hypopituitarism but is controversial in adults.

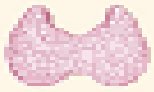
SHEEHAN SYNDROME

* SUSPECTED in THOSE WHO JUST GAVE BIRTH and PRESENT with:

- FAILURE to LACTATE
&
- ABSENT MENSTRUATION

→ PROLACTIN DEFICIENCY

* FEATURES of HYPOPITUITARISM
- HYPOTHYROIDISM
or
- CORTISOL DEFICIENCY

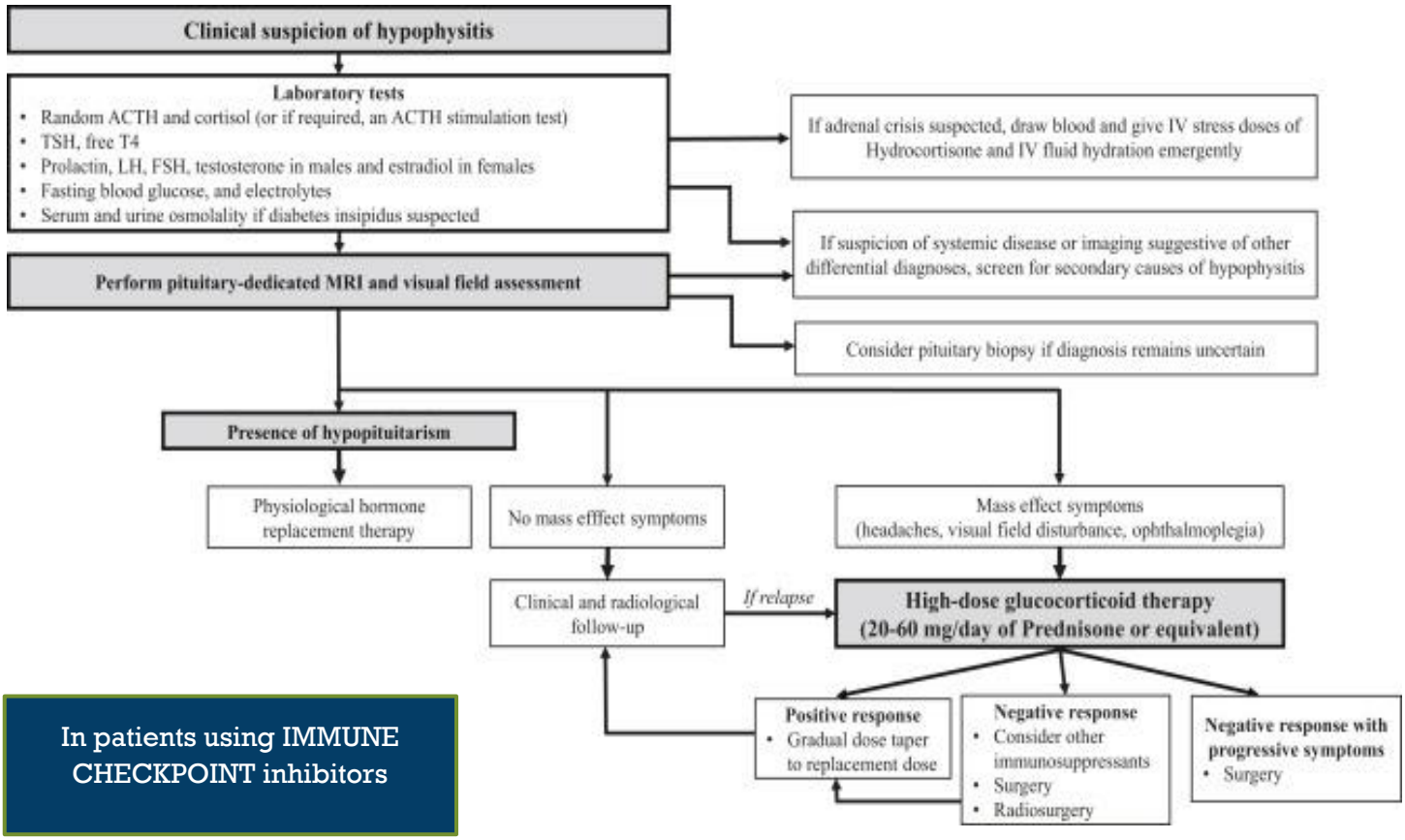


→ DEPENDING on EXTENT of NECROSIS

Feature	Sheehan's syndrome	Lymphocytic hypophysitis
Epidemiology	Common in developing nations	Common in developed nations
Gender	Women only	Men, women and children
Association with other autoimmune disorders	Uncommon	Common
Parity	Follows only pregnancy	Can occur without pregnancy
Postpartum hemorrhage	Common precipitating factor	Not required
Common trophic hormone deficiencies	Lactotroph, somatotroph, thyrotroph	Corticotroph, thyrotroph
Common hormone preservation	Gonadotroph, corticotroph	Somatotroph, gonadotroph
Hyperprolactinemia	Rare	Common
Diabetes insipidus	Rare	Common
Pituitary MRI	Empty sella	Pituitary mass

MRI: Magnetic resonance imaging

Pituitary disorders; Management of lymphocytic hypophysitis


Clinical suspicion of hypophysitis
Laboratory tests
• Random ACTH and cortisol (or if required, an ACTH stimulation test)
• TSH, free T4
• Prolactin, LH, FSH, testosterone in males and estradiol in females
• Fasting blood glucose, and electrolytes
• Serum and urine osmolality if diabetes insipidus suspected
If adrenal crisis suspected, draw blood and give IV stress doses of Hydrocortisone and IV fluid hydration emergently
If suspicion of systemic disease or imaging suggestive of other differential diagnoses, screen for secondary causes of hypophysitis
Perform pituitary-dedicated MRI and visual field assessment
Consider pituitary biopsy if diagnosis remains uncertain
Presence of hypopituitarism
Physiological hormone replacement therapy
No mass efffect symptoms
Mass effect symptoms (headaches, visual field disturbance, ophthalmoplegia)
Clinical and radiological follow-up
If relapse
High-dose glucocorticoid therapy (20-60 mg/day of Prednisone or equivalent)
Positive response
• Gradual dose taper to replacement dose
Negative response
• Consider other immunosuppressants
• Surgery
• Radiosurgery
Negative response with progressive symptoms
• Surgery

In patients using IMMUNE CHECKPOINT inhibitors

Clinical suspicion of hypophysitis: symptoms and signs

Early: headache, visual impairment, nausea, vomiting, loss of appetite, fatigue, weakness, asthenia, fever, lethargy, hypotension, hypoglycemia, hyponatremia, eosinophilia.

Late: amenorrhea, impotence, coma.

Consider adrenal insufficiency*

Diagnostic tests: Brain MRI; blood pressure; ECG; glycemia, plasma osmolarity, electrolytes, blood cell count, ACTH, TSH, IGF-I, FSH, LH, ADH, plasma cortisol, fT4, prolactin; testosterone/estradiol; visual field.

Endocrinology consultation

Clinical diagnosis of hypophysitis

YES

- Pause anti–CTLA-4 mAb
- HD corticosteroids (DEX 4 mg/ 6 hours) then taper down according to evolution of symptoms
- Hormone replacement therapy under endocrinological surveillance
- Repeat lab tests and brain MRI

- Residual toxicity grade ≤2

OR

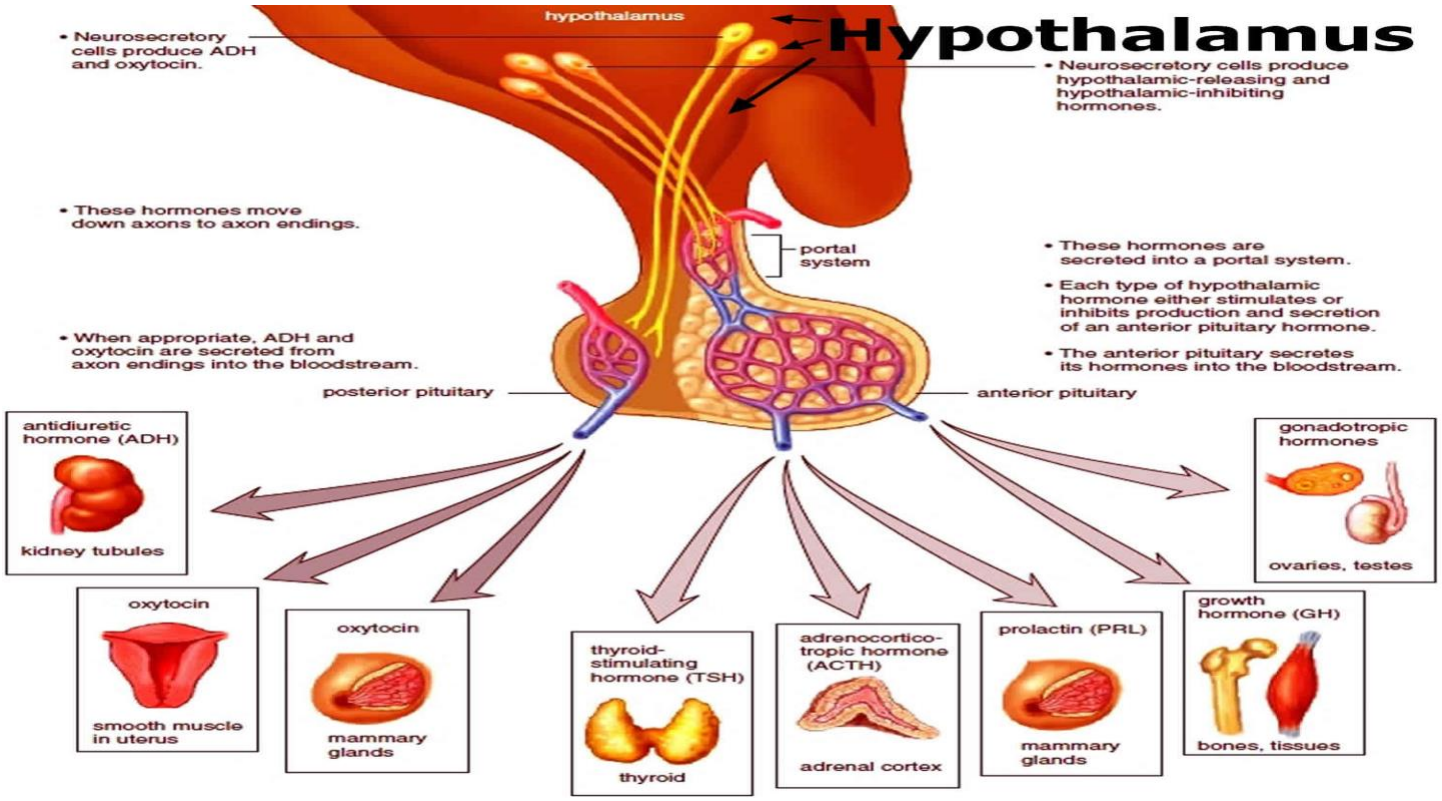
- Ability to reduce DEX to ≤1 mg per day or equivalent

yes → Restart anti–CTLA-4 mAb

no → Consider discontinuation of anti–CTLA-4 mAb

NO

- Rule out other causes (e.g., sepsis)
- Repeat lab tests within 1-3 weeks


Hypothalamus
hypothalamus
• Neurosecretory cells produce ADH and oxytocin.
• Neurosecretory cells produce hypothalamic-releasing and hypothalamic-inhibiting hormones.
• These hormones move down axons to axon endings.
portal system
• These hormones are secreted into a portal system.
• Each type of hypothalamic hormone either stimulates or inhibits production and secretion of an anterior pituitary hormone.
• The anterior pituitary secretes its hormones into the bloodstream.
• When appropriate, ADH and oxytocin are secreted from axon endings into the bloodstream.
posterior pituitary
anterior pituitary
antidiuretic hormone (ADH)
kidney tubules
gonadotropic hormones
ovaries, testes
oxytocin
smooth muscle in uterus
oxytocin
mammary glands
thyroid-stimulating hormone (TSH)
thyroid
adrenocortico-tropic hormone (ACTH)
adrenal cortex
prolactin (PRL)
mammary glands
growth hormone (GH)
bones, tissues

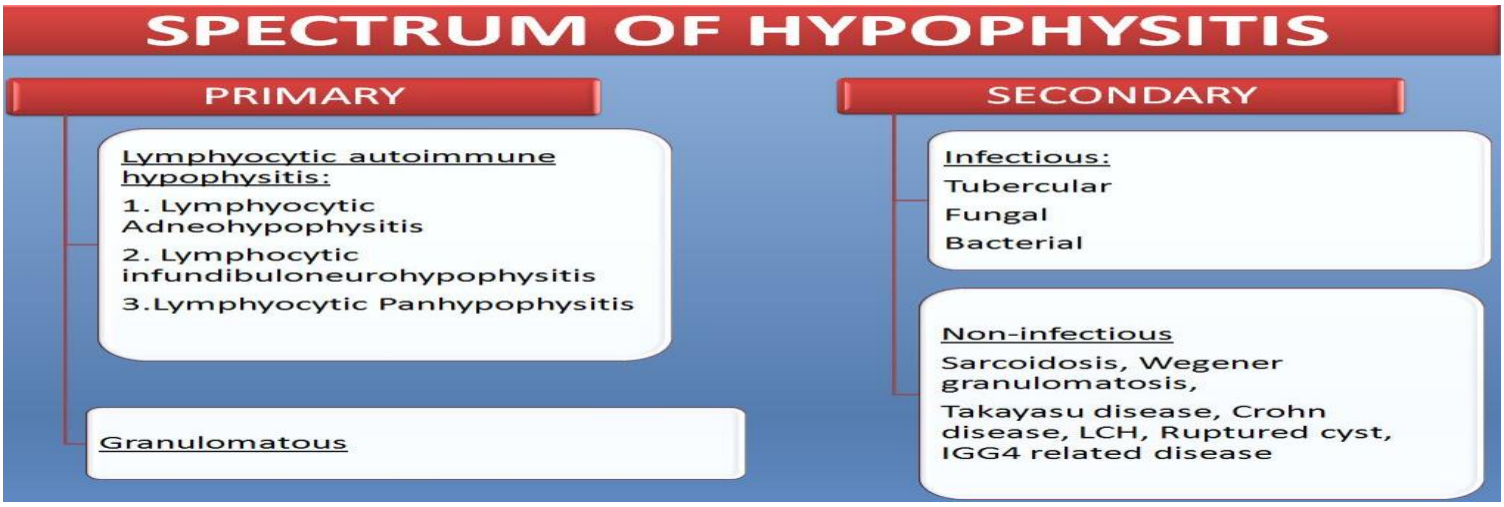
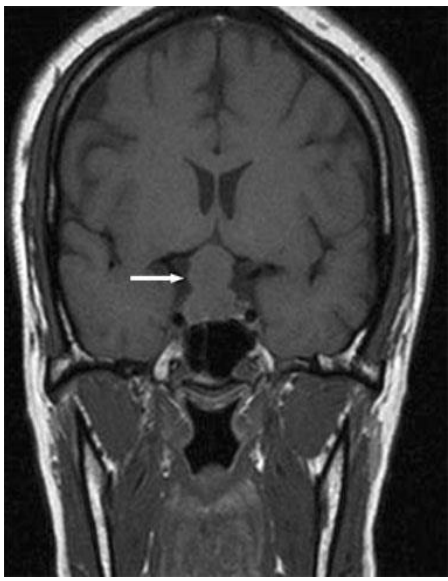


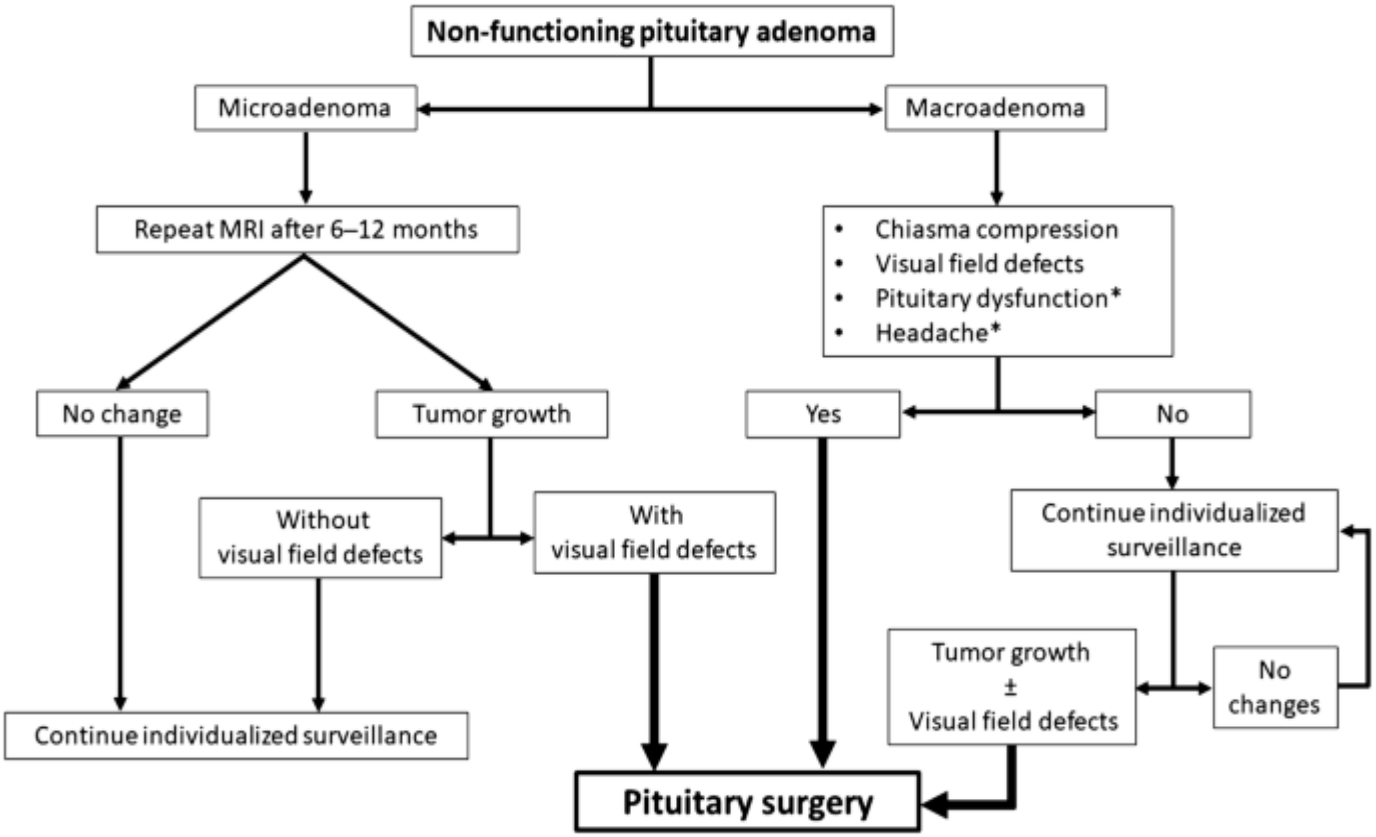
Table 1: Comparison of radiological findings seen in Lymphocytic Hypophysitis and Pituitary Adenoma as seen on MRI

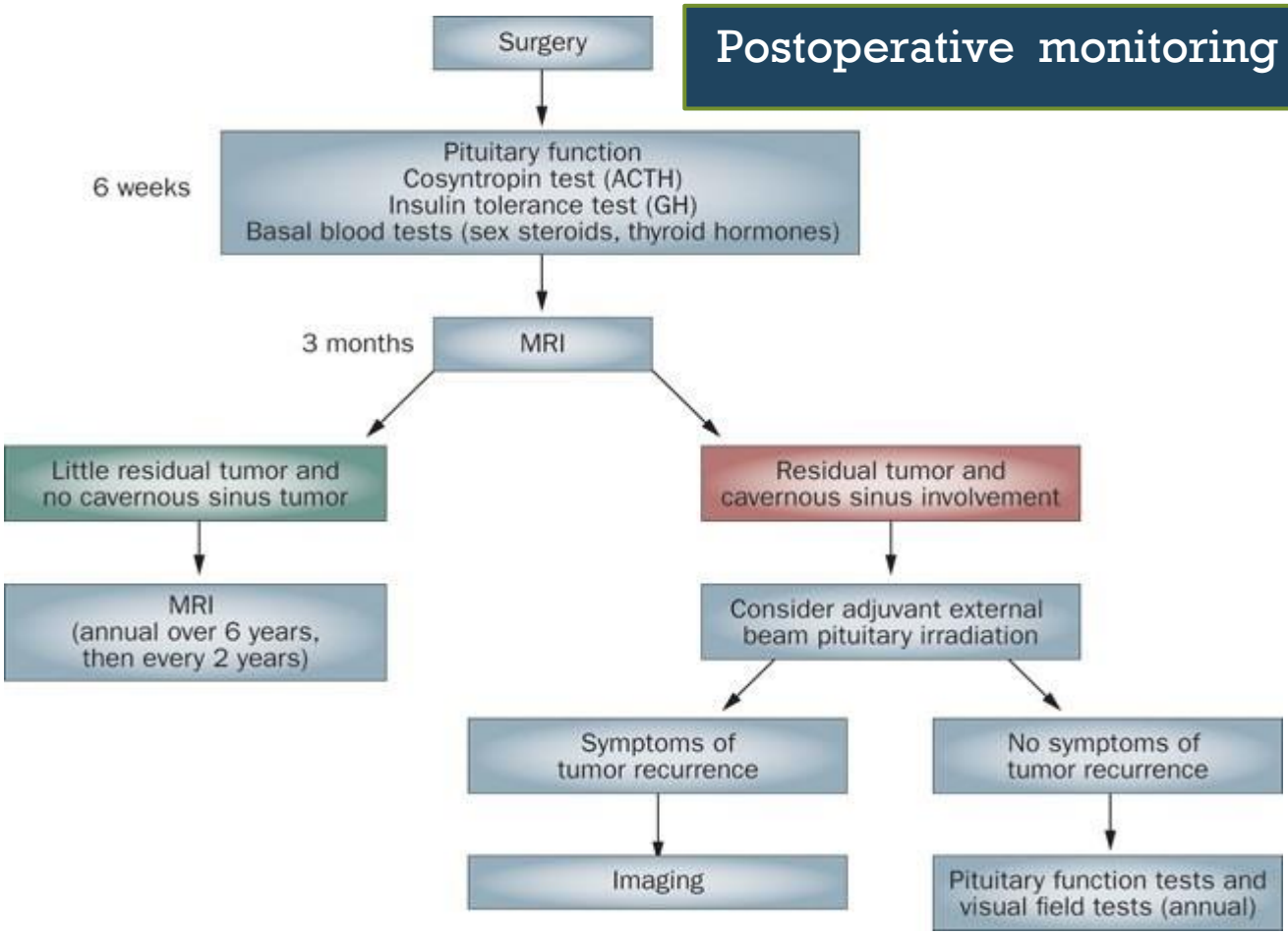
Typical Radiological Findings	Pituitary Adenoma	Lymphocytic Hypophysitis
Gland Enlargement	Asymmetrical	Symmetrical
Pituitary Stalk Thickening	Absent	Usually present
Pituitary Stalk Position	Deviation	Usually central
Sellar Floor Involvement	Can be seen occasionally	Rarely seen
Post gadolinium enhancement	Enhancement usually heterogenous	Diffuse and homogenous enhancement seen
Posterior Pituitary Signal	Usually present	Usually absent



Pituitary disorders; Management of Pituitary mass

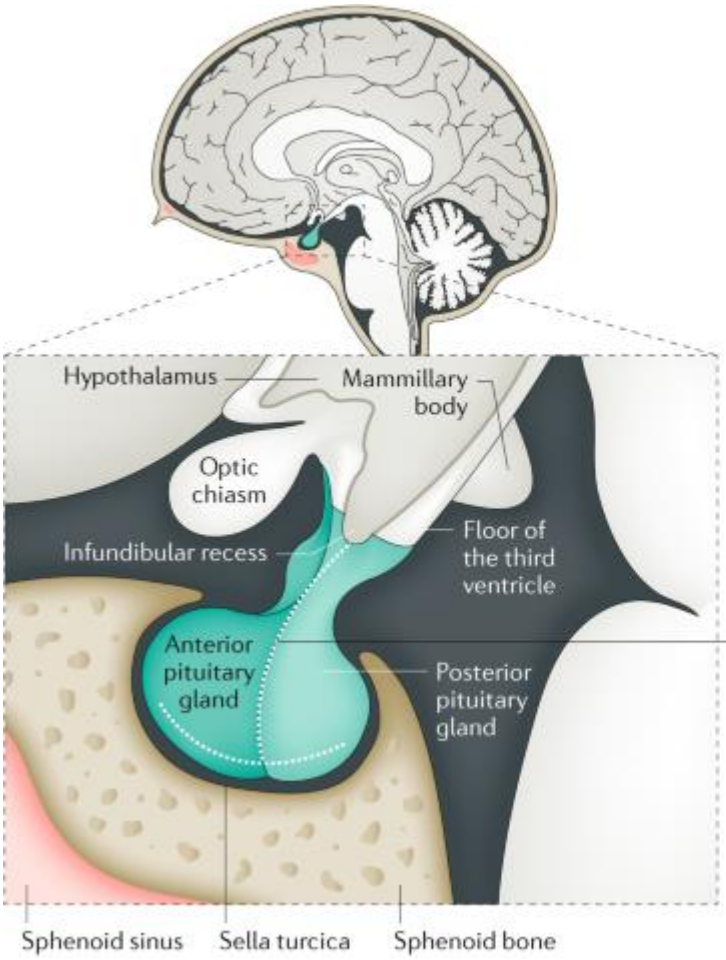
History taking and Examination is essential to assess Pituitary functions (PRL,TSH, FT4. FSH,LH , E2, Free testosterone, IGF=1, Scortisol 9am 9pm)




Surgery
Postoperative monitoring
6 weeks
Pituitary function
Cosyntropin test (ACTH)
Insulin tolerance test (GH)
Basal blood tests (sex steroids, thyroid hormones)
3 months
MRI
Little residual tumor and no cavernous sinus tumor
Residual tumor and cavernous sinus involvement
MRI (annual over 6 years, then every 2 years)
Consider adjuvant external beam pituitary irradiation
Symptoms of tumor recurrence
No symptoms of tumor recurrence
Imaging
Pituitary function tests and visual field tests (annual)

Pituitary disorders; Management of Craniopharyngioma

Remember : It Also occurs in Adults



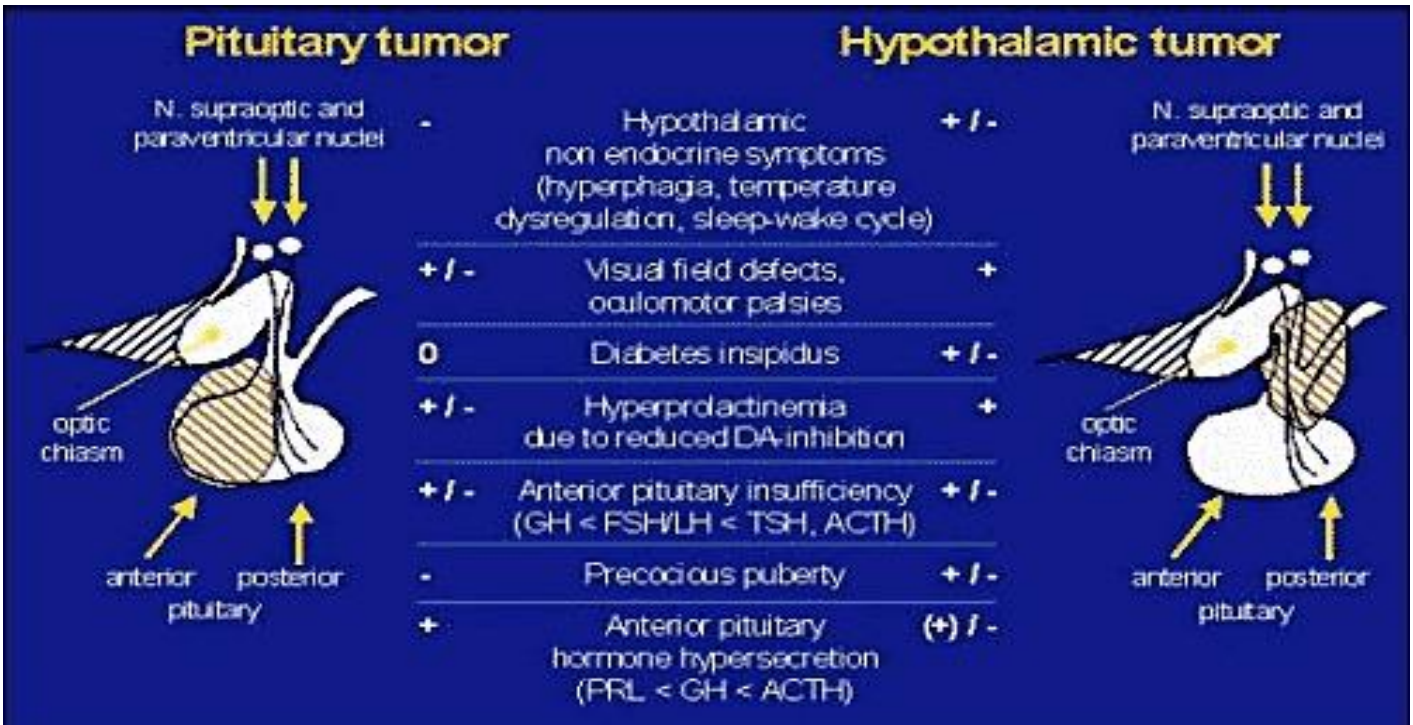
ACPs

- Age of presentation: bimodal peaks at 5–15 and 45–60 years
- Cell of origin: embryonic remnants of the Rathke's pouch epithelium
- Appearance on MRI: cauliflower-like shape with ~90% calcifications, ~90% enhancement and ~90% cysts, containing cholesterol-rich oily fluid
- Pathological features: distinctive epithelium that forms stellate reticulum, wet keratin and basal palisades
- Key symptomology: visual impairment, headache and endocrine deficiencies

PCPs

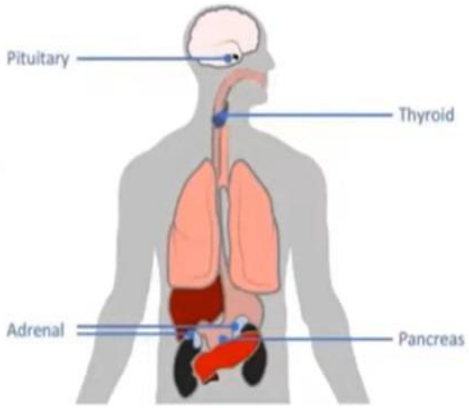
- Age of presentation: 40–55 years
- Cell of origin: embryonic remnants of the Rathke's pouch epithelium
- Appearance on MRI: mostly solid, rarely cystic and without calcifications
- Pathological features: fibrovascular cores lined by non-keratizing squamous epithelium
- Key symptomology: headache and hypothalamic symptoms, including psychiatric alterations

HOW to Differentiate between pituitary origin tumors and hypothalamic tumors

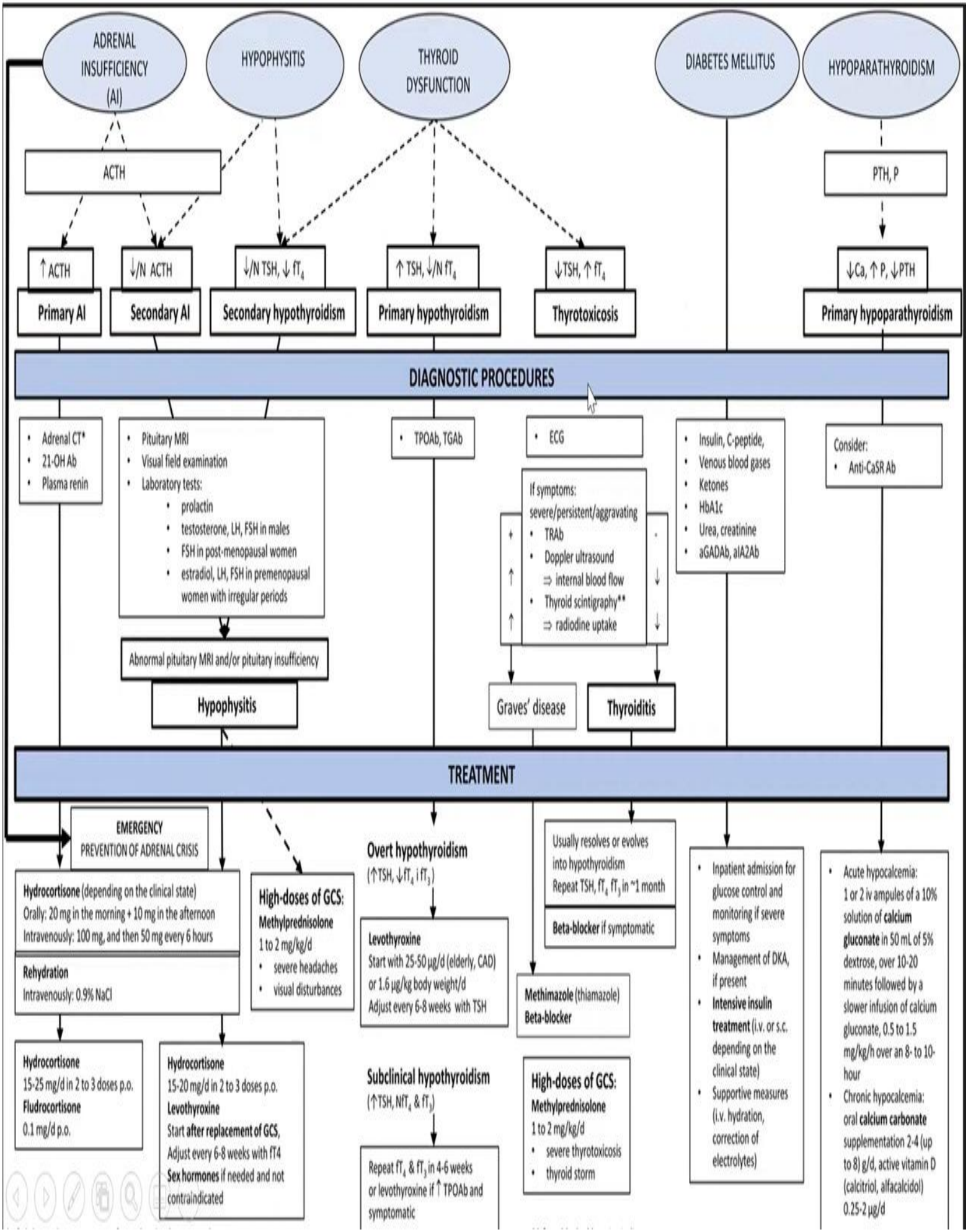

Pituitary tumor
Hypothalamic tumor
N. supraoptic and paraventricular nuclei
optic chiasm
anterior pituitary
posterior pituitary
- Hypothalamic non endocrine symptoms (hyperphagia, temperature dysregulation, sleep-wake cycle) +/-
+/- Visual field defects, oculomotor palsies +
0 Diabetes insipidus +/-
+/- Hyperprolactinemia due to reduced DA-inhibition +
+/- Anterior pituitary insufficiency (GH < FSH/LH < TSH, ACTH) +/-
- Precocious puberty +/-
+ Anterior pituitary hormone hypersecretion (PRL < GH < ACTH) (+) /-
N. supraoptic and paraventricular nuclei
optic chiasm
anterior pituitary
posterior pituitary

Endocrine Immune-related Adverse Events

- Common
  - Thyroid
    - Hyperthyroidism
    - Hypothyroidism
    - Thyroiditis (uncommon)
  - Pituitary (~10% with Ipilimumab, rare with PD-1 Inhibitors)
    - Hypophysitis
    - Hypopituitarism
- Uncommon/rare
  - Adrenal insufficiency
  - Type 1 diabetes mellitus/ diabetic ketoacidosis



Unlike most other immune related toxicities, endocrine adverse events frequently do not resolve and result in permanent hormone deficiency


ADRENAL INSUFFICIENCY (AI)
HYPOPHYSITIS
THYROID DYSFUNCTION
DIABETES MELLITUS
HYPOPARATHYROIDISM
ACTH
PTH, P
↑ ACTH
↓/N ACTH
↓/N TSH, ↓ fT4
↑ TSH, ↓/N fT4
↓TSH, ↑ fT4
↓Ca, ↑ P, ↓PTH
Primary AI
Secondary AI
Secondary hypothyroidism
Primary hypothyroidism
Thyrotoxicosis
Primary hypoparathyroidism
DIAGNOSTIC PROCEDURES
Adrenal CT*
21-OH Ab
Plasma renin
Pituitary MRI
Visual field examination
Laboratory tests:
prolactin
testosterone, LH, FSH in males
FSH in post-menopausal women
estradiol, LH, FSH in premenopausal women with irregular periods
TPOAb, TGAb
ECG
If symptoms: severe/persistent/aggravating
TRAb
Doppler ultrasound ⇒ internal blood flow
Thyroid scintigraphy** ⇒ radiodine uptake
Insulin, C-peptide,
Venous blood gases
Ketones
HbA1c
Urea, creatinine
aGADAb, aIA2Ab
Consider:
Anti-CaSR Ab
Abnormal pituitary MRI and/or pituitary insufficiency
Hypophysitis
Graves' disease
Thyroiditis
TREATMENT
EMERGENCY
PREVENTION OF ADRENAL CRISIS
Hydrocortisone (depending on the clinical state)
Orally: 20 mg in the morning + 10 mg in the afternoon
Intravenously: 100 mg, and then 50 mg every 6 hours
Rehydration
Intravenously: 0.9% NaCl
High-doses of GCS:
Methylprednisolone
1 to 2 mg/kg/d
severe headaches
visual disturbances
Overt hypothyroidism
(↑TSH, ↓fT4 i fT3)
Levothyroxine
Start with 25-50 µg/d (elderly, CAD) or 1.6 µg/kg body weight/d
Adjust every 6-8 weeks with TSH
Usually resolves or evolves into hypothyroidism
Repeat TSH, fT4 fT3 in ~1 month
Beta-blocker if symptomatic
Methimazole (thiamazole)
Beta-blocker
Inpatient admission for glucose control and monitoring if severe symptoms
Management of DKA, if present
Intensive insulin treatment (i.v. or s.c. depending on the clinical state)
Supportive measures (i.v. hydration, correction of electrolytes)
Acute hypocalcemia: 1 or 2 iv ampules of a 10% solution of calcium gluconate in 50 mL of 5% dextrose, over 10-20 minutes followed by a slower infusion of calcium gluconate, 0.5 to 1.5 mg/kg/h over an 8- to 10-hour
Chronic hypocalcemia: oral calcium carbonate supplementation 2-4 (up to 8) g/d, active vitamin D (calcitriol, alfacalcidol) 0.25-2 µg/d
Hydrocortisone
15-25 mg/d in 2 to 3 doses p.o.
Fludrocortisone
0.1 mg/d p.o.
Hydrocortisone
15-20 mg/d in 2 to 3 doses p.o.
Levothyroxine
Start after replacement of GCS,
Adjust every 6-8 weeks with fT4
Sex hormones if needed and not contraindicated
Subclinical hypothyroidism
(↑TSH, NfT4 & fT3)
Repeat fT4 & fT3 in 4-6 weeks or levothyroxine if ↑ TPOAb and symptomatic
High-doses of GCS:
Methylprednisolone
1 to 2 mg/kg/d
severe thyrotoxicosis
thyroid storm

Calcium disorders; Management of hypocalcemia

Hypocalcemia

CLINICAL MANIFESTATION

SERUM CALCIUM PHYSIOLOGICAL RANGE: 8.5 – 10.5 mg/dL

Neuromuscular
Numbness, tingling, tetany, spasm
- Perioral area
- Muscles
- Laryngospasms

Cardiac
- Prolonged QTc
- ST segment Elevation
- Mimics Myocardial Infarct

Neuronal
- Seizures

"CATTS go Numb" (Convulsion, Arrhythmia, Tingling, Tetany, Spasms, Numbness)

PHYSICAL EXAM

CHVOSTEK'S
Tapping facial nerve → facial muscle spasms

TROUSSEAU'S
Occlusion of brachial a. with BP cuff → carpal muscle spasms

↓ Ca^{2+} < 8.5

*Pearl: Alkalemia causes transient hypocalcemia
- Less ionized calcium relative to bound

↑ PTH

PTH

PTH INDEPENDENT

LOW VIT D
Deficiency
- ↓ Exposure (sunlight)
- ↓ Intake (diet)

Activation
- Liver disease
- Kidney Disease (CKD)

Metabolism
- Drugs (phenytoin)

NORMAL VIT D
Accelerated Bone Formation
- Hungy Bone Syndrome

Calcium Sequestration
- Pancreatitis
- Blood Transfusions

Medications
- Bisphosphonates
- Denosumab

PTH DEPENDENT

INADEQUATE PTH
Iatrogenic*
- Surgery, Radiation

Mg^{+} deficiency

Infiltrative
- Amyloid
- TB (granuloma)

Autoimmune
- APS 1

↓ PTH

DiGeorge Syndrome

* - MOST COMMON

PTH RESISTANCE
Pseudohypoparathyroidism
- Alteration in PTH Signaling

↑ PTH

EVALUATION

1ST = Repeat calcium & correct for albumin

LABS
- Calcium [8.5 - 10.5]
- PTH
- Albumin
- Ionized Ca^{2+}
- 25-hydroxyvitamin D
- Mg^{+}
- Phosphate

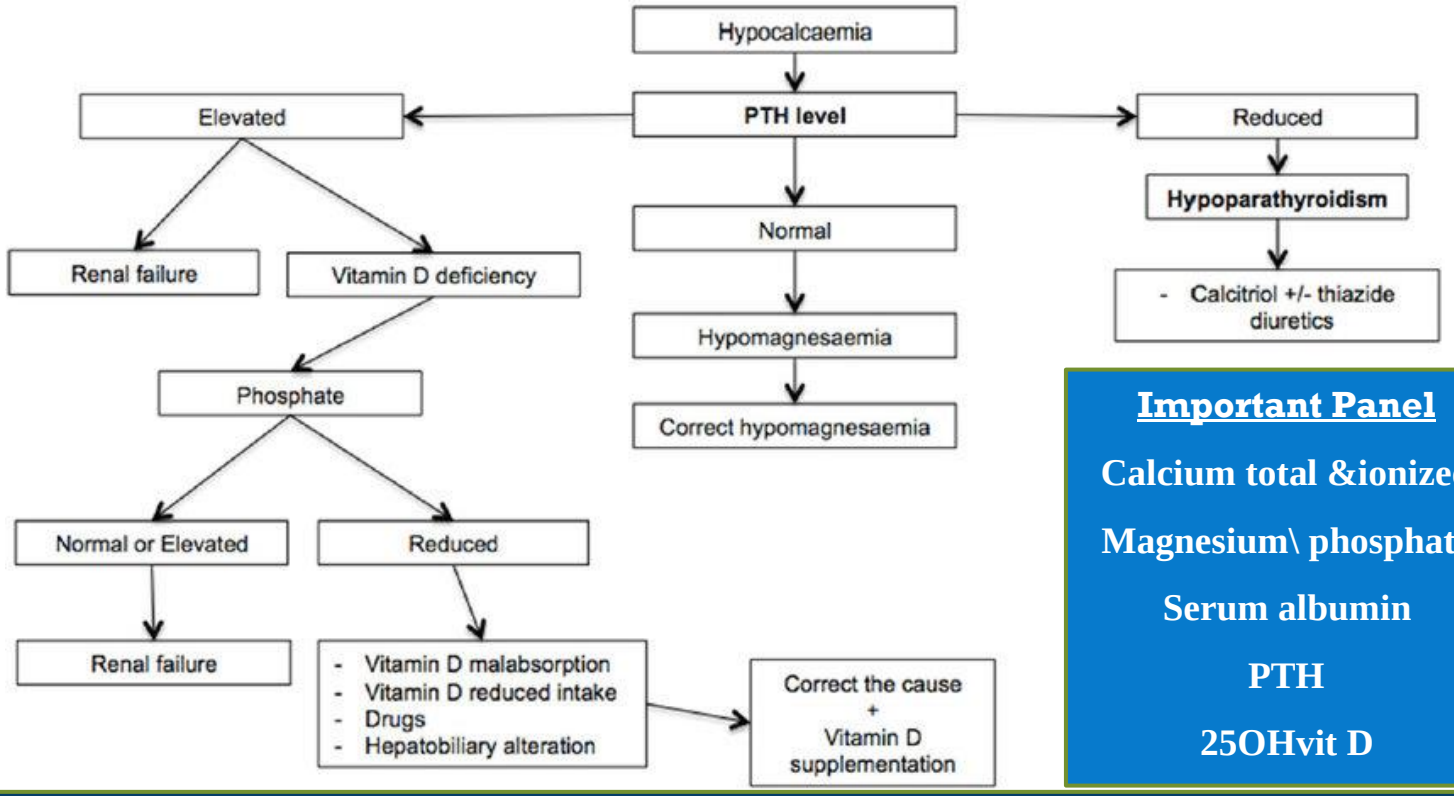
MANAGEMENT GUIDED BY DEGREE OF HYPOCALCEMIA, TEMPO AND THE PATIENT'S SYMPTOMS

SEVERE - Ca^{2+} <7.5 mg/dL / ionized Ca^{2+} <1 mg/dL
Symptoms: e.g. - Tetany
Treatment: IV Calcium gluconate, 1-2g over 10-20min

MILD - Ca^{2+} >7.5 mg/dL
Symptoms: e.g. - Perioral numbness
Treatment: PO Ca^{2+} and calcitriol

Address the underlying cause of ↓ Ca^{2+}:
- Concomitant vitamin D deficiency - Supplement
- CKD - Supplement calcitriol to bypass renal activation of vitamin D synthesis

Calcium disorders; Management of hypocalcemia



Important Panel

Calcium total &ionized

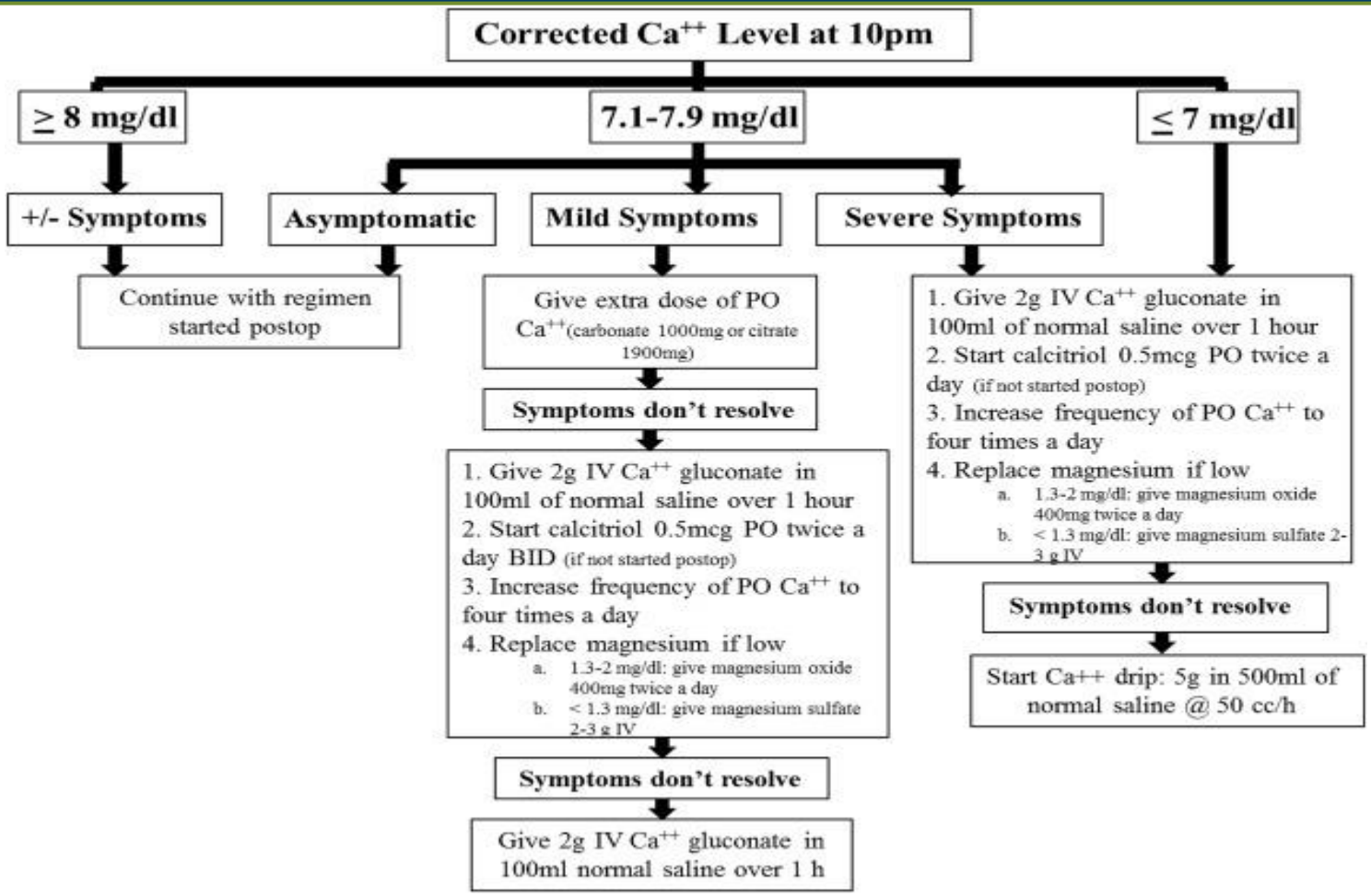
Magnesium\ phosphate

Serum albumin

PTH

25OHvit D

Management of hypocalcemia after thyroid surgery


Corrected Ca++ Level at 10pm
≥ 8 mg/dl
7.1-7.9 mg/dl
≤ 7 mg/dl
+/- Symptoms
Asymptomatic
Mild Symptoms
Severe Symptoms
Continue with regimen started postop
Give extra dose of PO Ca++ (carbonate 1000mg or citrate 1900mg)
Symptoms don't resolve
1. Give 2g IV Ca++ gluconate in 100ml of normal saline over 1 hour
2. Start calcitriol 0.5mcg PO twice a day BID (if not started postop)
3. Increase frequency of PO Ca++ to four times a day
4. Replace magnesium if low
a. 1.3-2 mg/dl: give magnesium oxide 400mg twice a day
b. < 1.3 mg/dl: give magnesium sulfate 2-3 g IV
Symptoms don't resolve
Give 2g IV Ca++ gluconate in 100ml normal saline over 1 h
1. Give 2g IV Ca++ gluconate in 100ml of normal saline over 1 hour
2. Start calcitriol 0.5mcg PO twice a day (if not started postop)
3. Increase frequency of PO Ca++ to four times a day
4. Replace magnesium if low
a. 1.3-2 mg/dl: give magnesium oxide 400mg twice a day
b. < 1.3 mg/dl: give magnesium sulfate 2-3 g IV
Symptoms don't resolve
Start Ca++ drip: 5g in 500ml of normal saline @ 50 cc/h

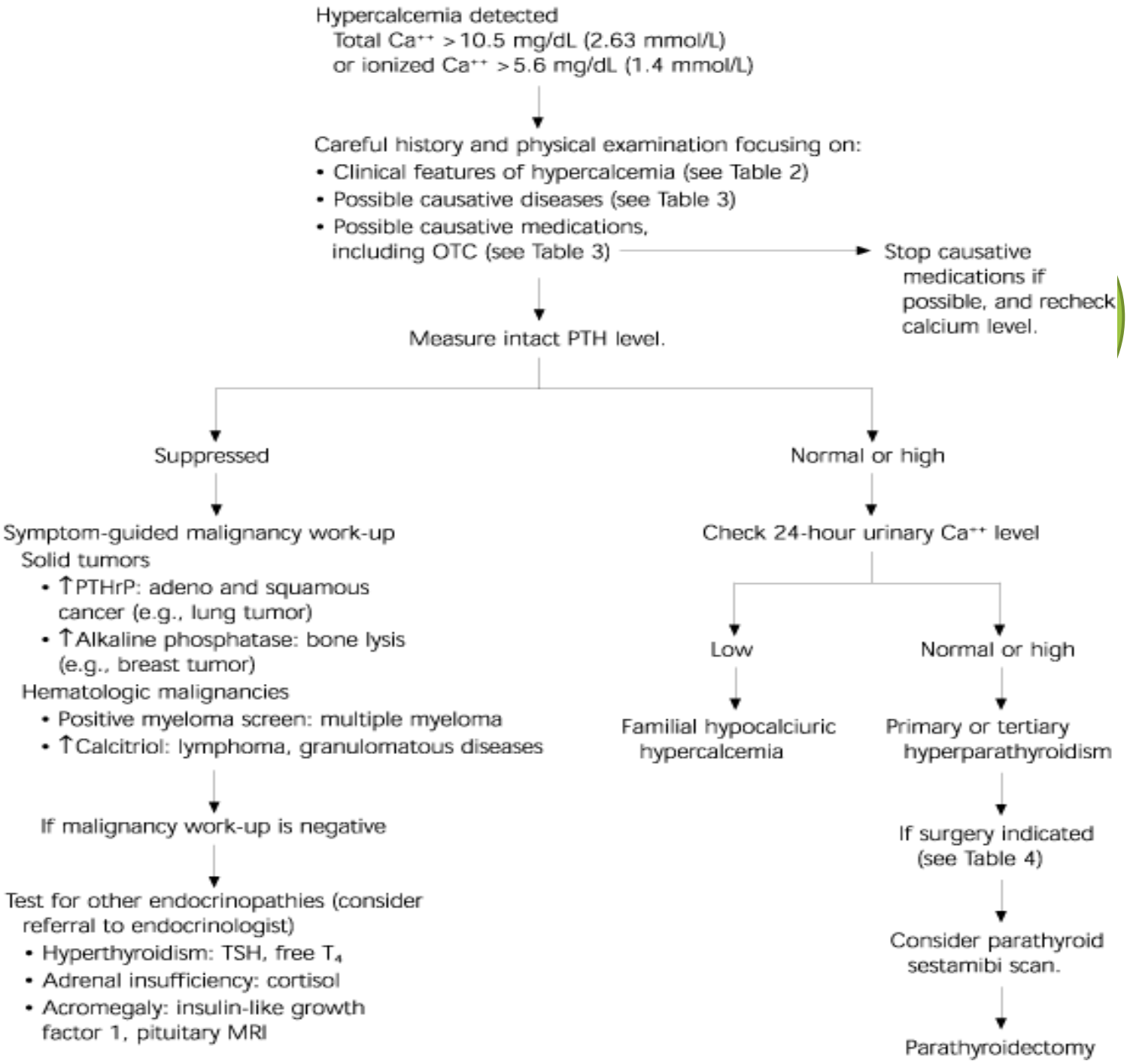
Calcium disorders; Management of hypocalcemia

How to Differentiate >>>>>

	Serum PTH	25-Hydroxyvitamin D	Alkaline phosphatase
Hypoparathyroidism	Low	Normal	Normal
PTH Resistance	High	Normal	Normal
Vitamin D Deficiency	High	Low	Normal or high
Vitamin D Resistance	High	Normal	Normal
Renal Disease	High	Normal or low	Normal or high
Hypomagnesemia	Normal	Normal or low	Normal
Metastatic Disease	High	Normal	High

Low PTH	Normal or High PTH
Congenital Abnormalities - DiGeorge Syndrome **Parathyroid Destruction** - Surgical - Autoimmune - Radiation - Metastases **Parathyroid Dysregulation** - Hypomagnesemia - Sepsis - CaSR receptor Defects	**Vitamin D Deficiency** - Renal Failure (↓ Production) - Nutritional (Malabsorption) - Vitamin D Resistance **PTH Resistance** - Hypomagnesemia **Increased Protein Binding** - Alkalosis **Drugs** - Bisphosphonates (↓Bone Resorption) - Phenytoin (Altered Metabolism) - Calcium Chelators - Citrate (Blood Products) **Medical Conditions** - Tumor Lysis Syndrome (Hyperphosphatemia) - Acute Pancreatitis - Rhabdomyolysis - Hungry Bone Syndrome - Coagulopathy - Osteoclastic Bone Metastasis

Calcium disorders; Management of hypercalcemia


Hypercalcemia detected
Total Ca++ >10.5 mg/dL (2.63 mmol/L)
or ionized Ca++ >5.6 mg/dL (1.4 mmol/L)
Careful history and physical examination focusing on:
• Clinical features of hypercalcemia (see Table 2)
• Possible causative diseases (see Table 3)
• Possible causative medications, including OTC (see Table 3)
Stop causative medications if possible, and recheck calcium level.
Measure intact PTH level.
Suppressed
Normal or high
Symptom-guided malignancy work-up
Solid tumors
• ↑PTHrP: adeno and squamous cancer (e.g., lung tumor)
• ↑Alkaline phosphatase: bone lysis (e.g., breast tumor)
Hematologic malignancies
• Positive myeloma screen: multiple myeloma
• ↑Calcitriol: lymphoma, granulomatous diseases
If malignancy work-up is negative
Test for other endocrinopathies (consider referral to endocrinologist)
• Hyperthyroidism: TSH, free T4
• Adrenal insufficiency: cortisol
• Acromegaly: insulin-like growth factor 1, pituitary MRI
Check 24-hour urinary Ca++ level
Low
Normal or high
Familial hypocalciuric hypercalcemia
Primary or tertiary hyperparathyroidism
If surgery indicated (see Table 4)
Consider parathyroid sestamibi scan.
Parathyroidectomy

Management of hypercalcemia of malignancy

Serum calcium	Severity	Management approach
10.5-11.9 mg/dL	Mild	If the patient is asymptomatic and hypercalcemia developed chronically, it may not require urgent treatment; can usually treat with isotonic fluids.
12.0-13.9 mg/dL	Moderate	Isotonic fluids alone are usually insufficient; can use calcitriol with bisphosphonate therapy.
>14 mg/dL	Severe	Should be treated even in patients without symptoms. Management is similar to moderate hypercalcemia. If >18 mg/dL, worsening renal failure, or inability to tolerate IV fluid, may need to consider dialysis.

MDedge News

Calcium disorders; Management of hypercalcemia

Table Pharmacologic Options for Hypercalcemia Associated with Cancer

Intervention	Mode of action	Dose	Adverse effects
Rehydration with NS followed by loop diuretics			
IV normal saline[1,2]	Enhances GFR and renal excretion of Ca^{2+}	200-500 mL/h or 2-4 L/d for 1-3 days depending on the patient's cardiovascular and renal status	Volume overload; may exacerbate heart failure
Furosemide[1,2]	Inhibits Ca^{2+} resorption in the renal tube	20-40 mg IV, after rehydration has been achieved	Hypokalemia, renal failure, and abnormalities of cardiac conduction
First-line medications: intravenous bisphosphonate			
Pamidronate[1,2,4]	Inhibits osteoclast activity; decreases bone resorption	60-90 mg IV over 2-4 hours as a single dose in a solution of 50-200 mL NS or D5W (allow at least 7 days before retreatment)	Nephrotoxicity; flulike symptoms with fever, chills, and headache
Zoledronic acid[1,2,5]		4 mg IV over 15 minutes in a solution of 50 mL NS or D5W	
Denosumab[6]	Inhibits RANKL to decrease osteoclast activity	120 mg SQ every 4 weeks; administer additional 120 mg on days 8 and 15 during the first month	Hypertension, fatigue, nausea, arthralgia, and hypocalcemia
Second-line medications			
Glucocorticoids[1,2]	Inhibits vitamin D conversion to calcitriol	Oral prednisone 20-40 mg/d for 10 days, intravenous hydrocortisone 200 mg daily for 3 days or equivalents	Immune suppression, myopathy, elevated blood glucose, weight gain, and elevated blood pressure
Calcitonin[9]	Inhibits bone resorption	4-8 IU/kg SQ or IM every 12 hours	May rebound; elevated Ca^{2+} after 24 hours; causes vomiting, cramps, and flushing
Gallium nitrate[1,2,7]	Inhibits osteoclast activity	Intravenous continuous infusion at 100-200 mg/m^2 over 24 hours for 5 days	Bone marrow suppression; nephrotoxicity

Ca^{2+} indicates calcium ions; D5W, 5% dextrose in water; GFR, glomerular filtration rate; IM, intramuscularly; IV, intravenously; NS, normal saline; RANKL, receptor activator of nuclear factor kappa-B ligand; SQ, subcutaneously.

Remember: The most common cause of hypercalcemia in hospital inpatients is malignancy and the most common cause of outpatiemt hypercalcemia is primary hyperparathyroidism

Calcium disorders; Management of hypercalcemia

Table 2. National Institutes of Health indications for parathyroidectomy in asymptomatic primary hyperparathyroidism
Less than 50 years old
Unable to be effectively followed up
Serum calcium >1.0 mg/dl above the normal range
Urinary calcium >400 mg/24hr
30% decrease in renal function
Complications of hyperparathyroidism: nephrocalcinosis, osteoporosis (T-score <2.5 standard deviation at lumbar spine, hip or wrist)
Severe psychoneurological disorder

hyperparathyroidism

	Primary hyperparathyroidism	Secondary hyperparathyroidism	Tertiary hyperparathyroidism
PTH	↑	↑	↑↑↑
Ca2+	↑ *	↓/N	↑
P04+	↓	↑/N	↑
Vitamin D	N/↓	↓↓↓	↓/N
Comments	In 85% a solitary parathyroid adenoma is present Important differential diagnosis is FHH (see Table 3)	Causes include: • chronic renal failure • vitamin D deficiency	Caused by: • end stage renal failure

* Differential diagnosis of hypercalcaemia includes drug induced (eg. lithium, thiazides) and hypercalcaemia of malignancy

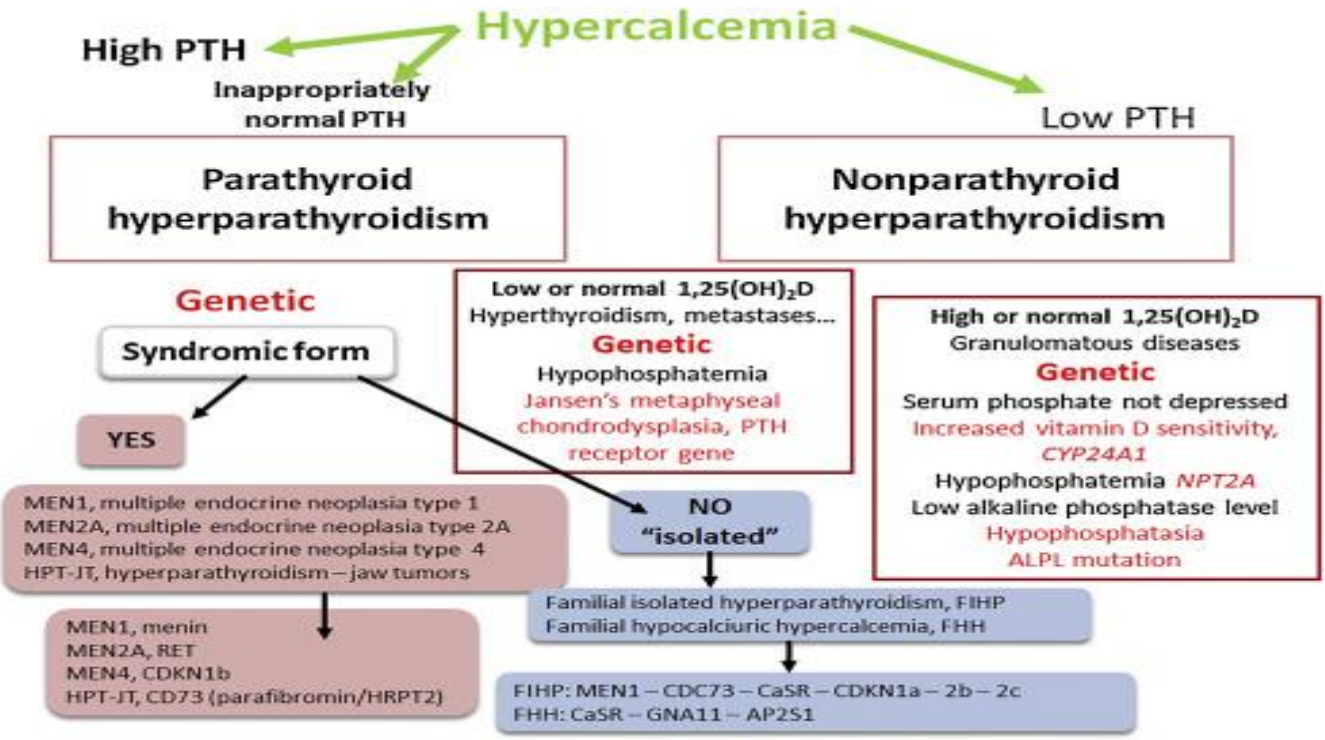
"VITAMINS TRAP"

Mnemonic for hypercalcemia:

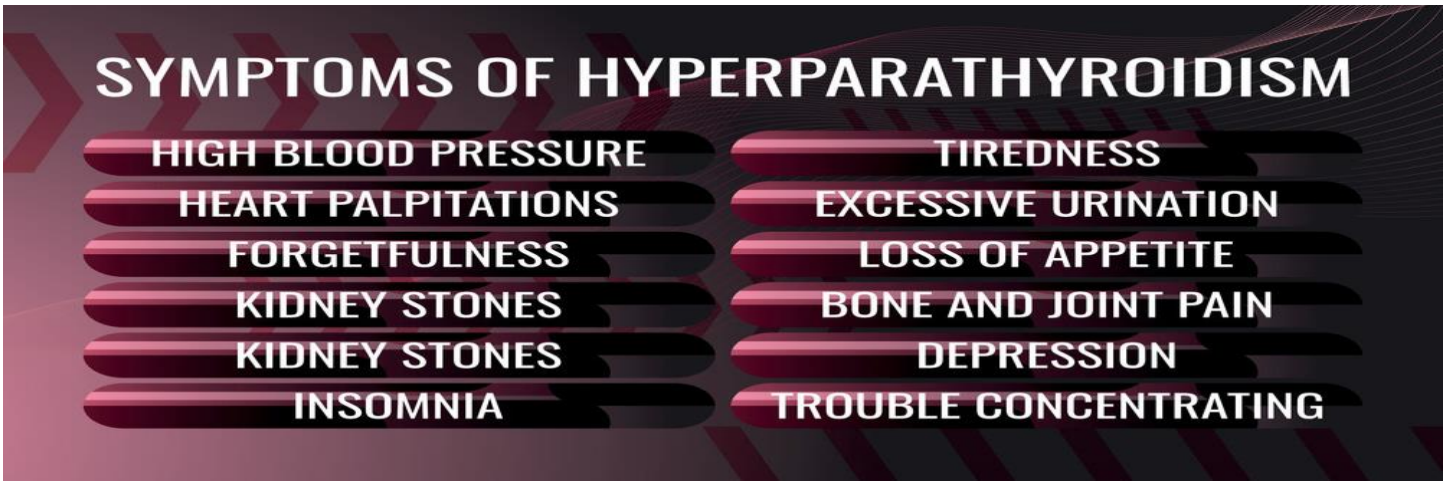
V= vitamins
I= immobilization
T= thyrotoxicosis
A= Addison's disease
M= milk-alkalai
I= inflammatory
N= neoplasm
S= sarcoidosis

T= thiazide diuretic
R= rhabdomyolysis
A= AIDS
P= Paget's of bone
Parenteral nutrition
Pheochromocytoma
Parathyroid

Calcium disorders; Management of hypercalcemia

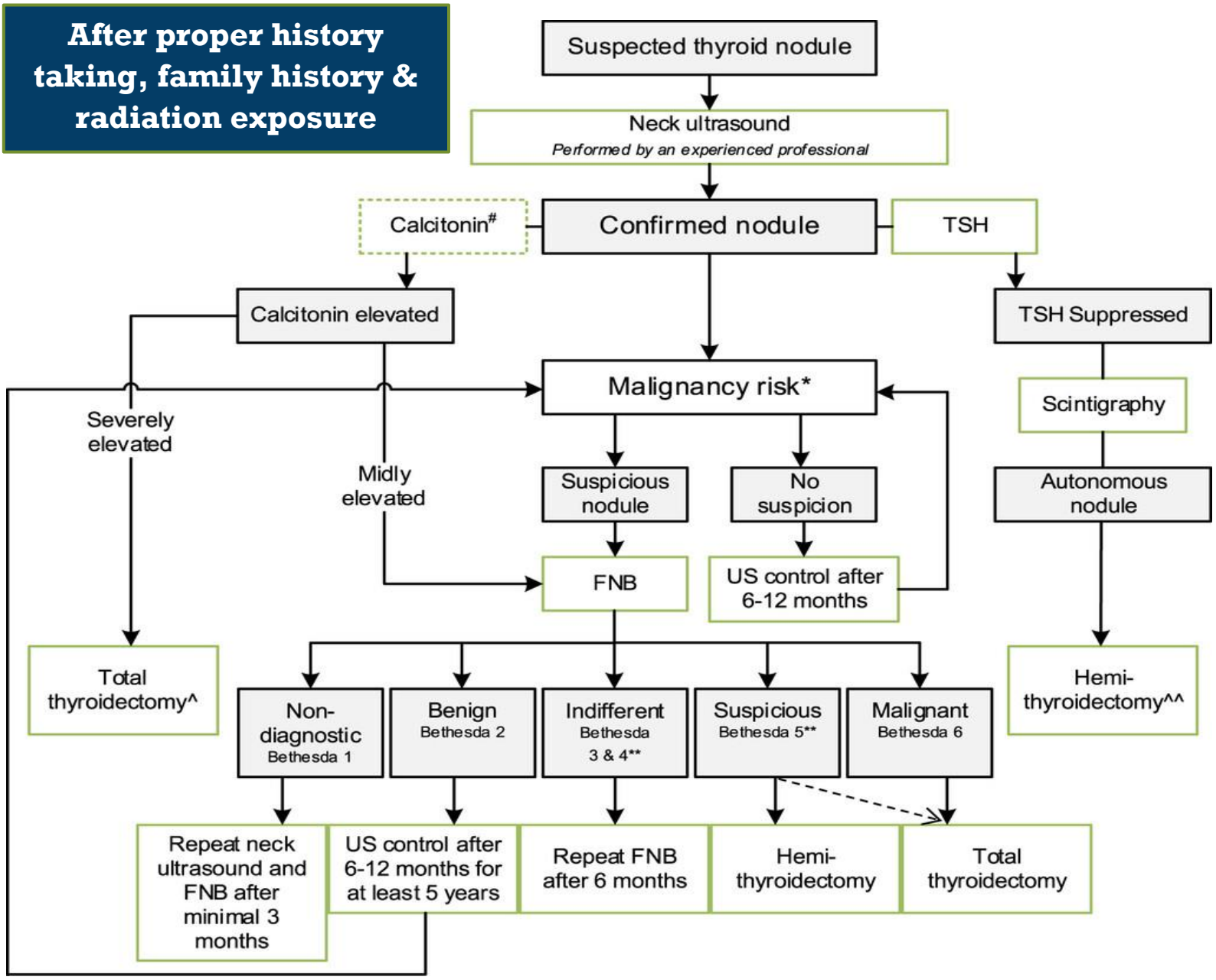


	Primary hyperparathyroidism	Familial hypocalciuric hypercalcaemia
Family history	Negative*	Positive
Fractional excretion of Ca2+	≥0.02	<0.01
Symptoms of hypercalcaemia	Maybe symptomatic	Asymptomatic
Parathyroid sestamibi scan	Usually shows a single parathyroid adenoma	No abnormal parathyroid tissue demonstrable



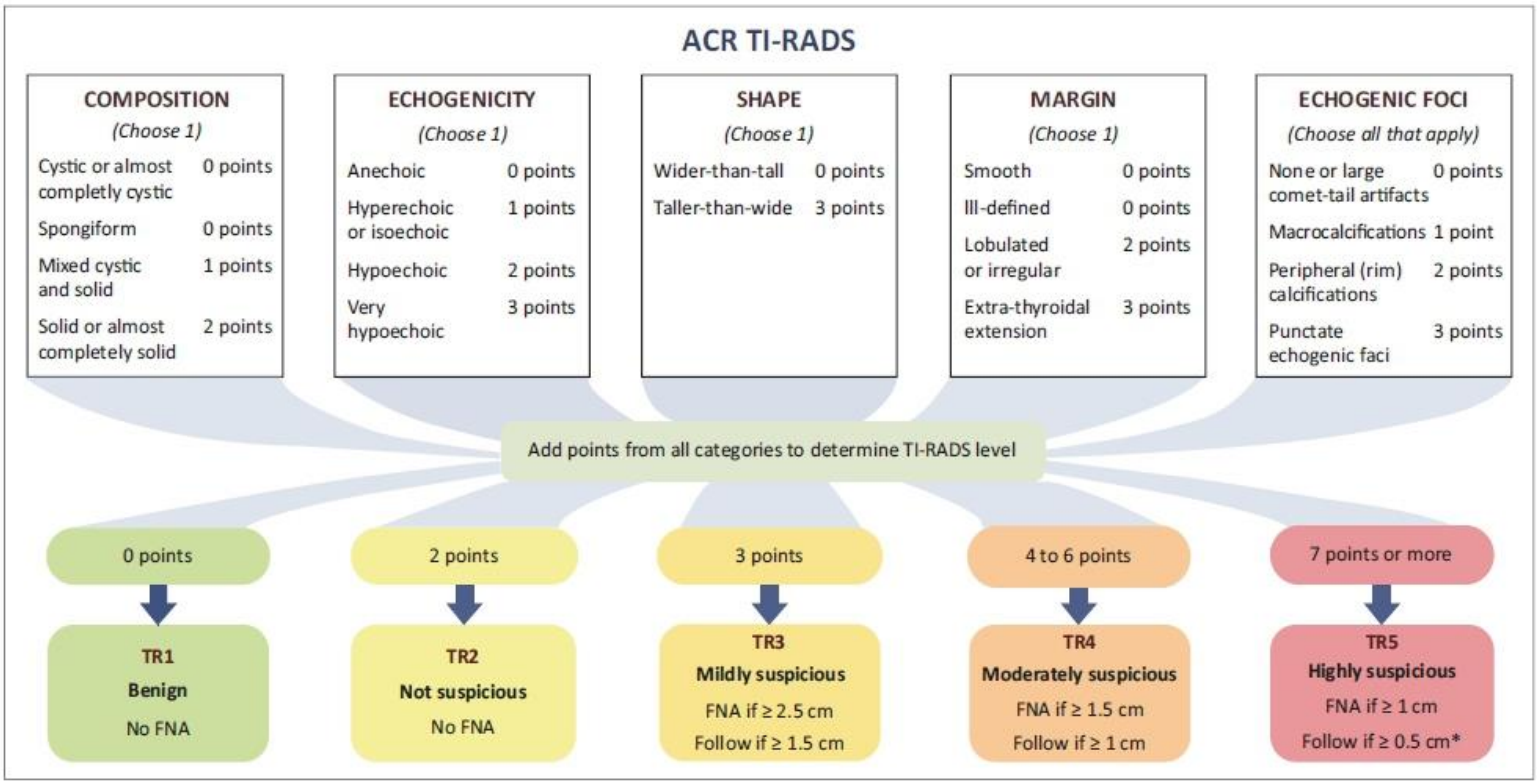
Thyroid disorders; Management of thyroid nodule

After proper history taking, family history & radiation exposure



Sonographic Pattern	Ultrasound Features	Estimated Risk of Malignancy	FNA Size Cutoff
High Suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE	>70% to 90%[a]	Recommend FNA at ‡ 1 cm
Intermediate Suspicion	Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape	10% to 20%	Recommend FNA at ‡ 1 cm
Low Suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETEc, or taller than wide shape.	5%–10%	Recommend FNA at ‡ 1.5 cm
Very Low Suspicion	Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns	<3%	Consider FNA at ‡ 2 cm Observation without FNA is also a reasonable option
Benign	Purely cystic nodules (no solid component)	<1%	No biopsy[b]

Thyroid disorders; Management of thyroid nodule

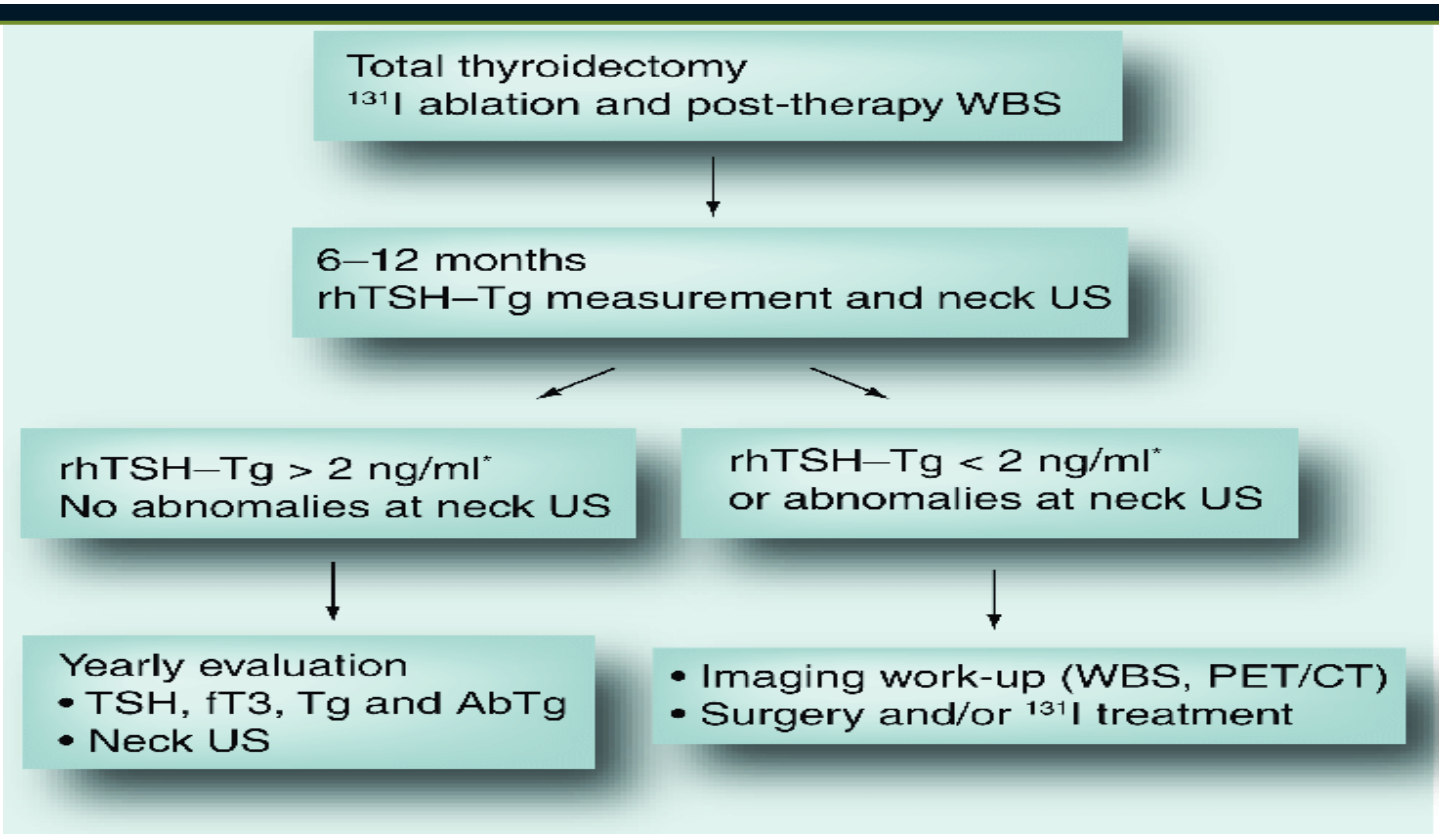


Source: Tessler FN, Middleton WD, Grant EG, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White paper of the ACR TI-RADS committee. J Am Coll Radiol. 2017;14(5):587–595. https://doi.org/10.1016/j.jacr.2017.01.046

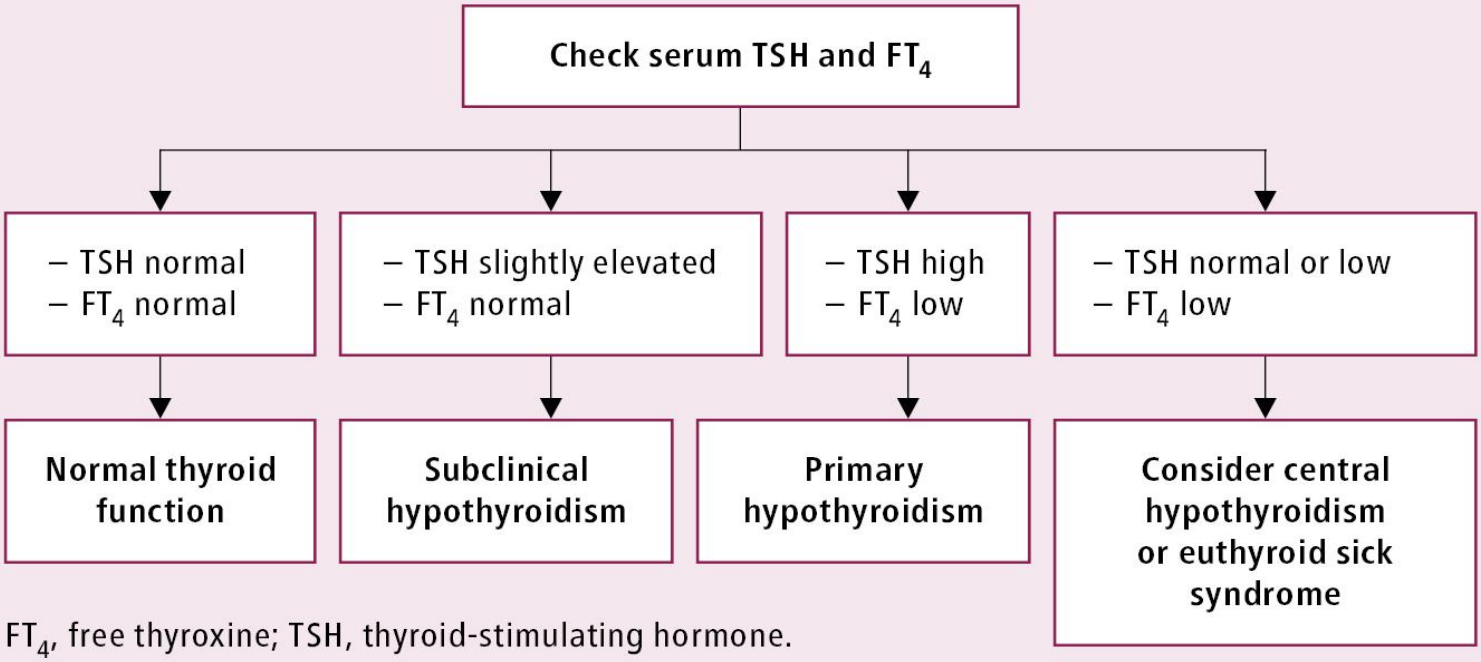
*, Refer to discussion of papillary microcarcinomas for 5–9 mm TR5 nodules.

FIGURE 1-A1: The American College of Radiology Thyroid Imaging Reporting and Data System.[11]

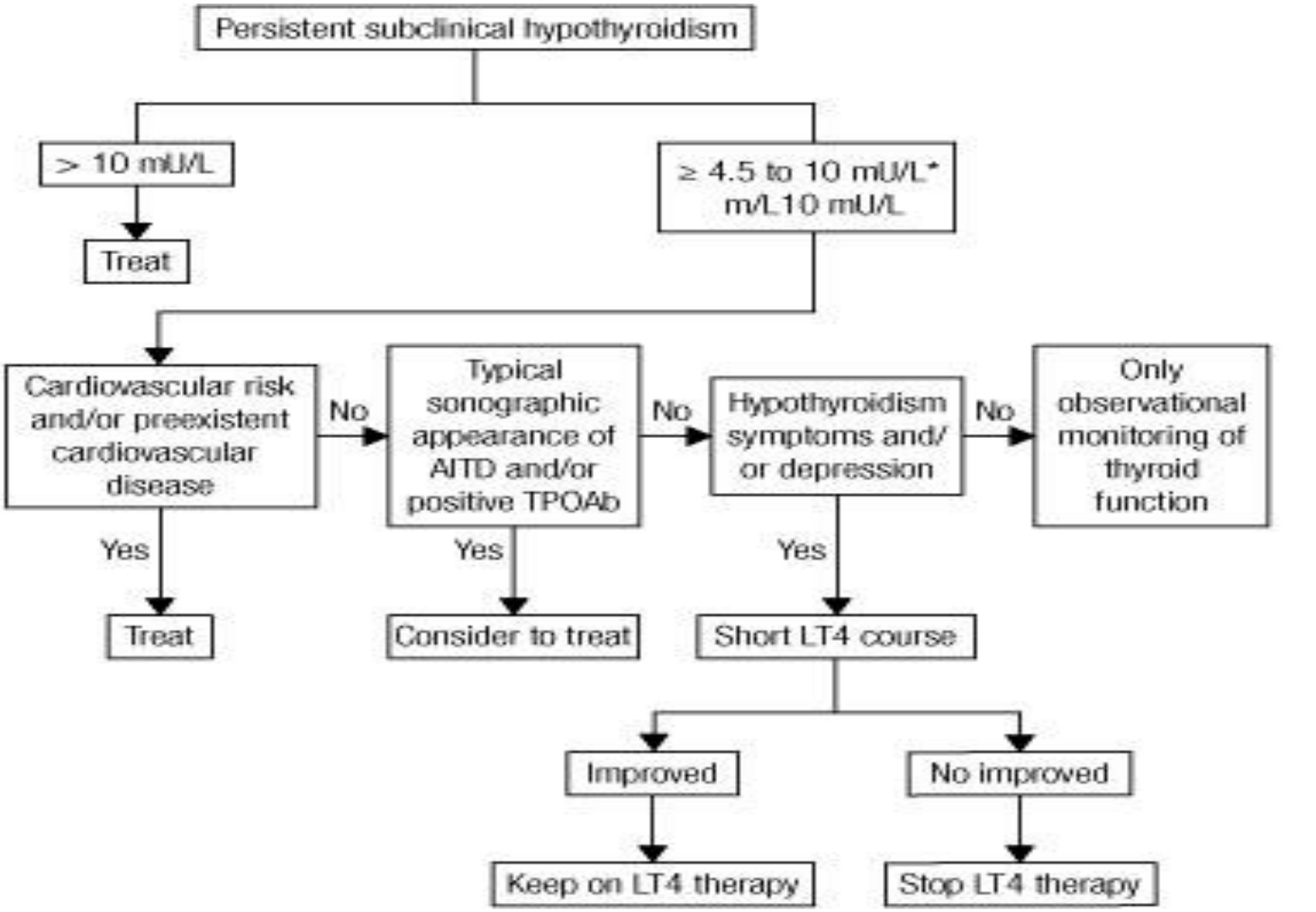
Thyroid cancer follow-up after (surgery and radioiodine ablation). * The rhTSH-Tg cut-off is 1 ng/ml in the European guidelines and 2 ng/ml in US guidelines. AbTg: Antibody thyroglobulin; fT3: free-tri-iodo-thyronine; rh: Recombinant human; Tg: Thyroglobulin; TSH: Thyroid stimulating hormone; US: Ultrasound; WBS: Whole body scan


Total thyroidectomy
131I ablation and post-therapy WBS
6–12 months
rhTSH–Tg measurement and neck US
rhTSH–Tg > 2 ng/ml*
No abnomalies at neck US
rhTSH–Tg < 2 ng/ml*
or abnomalies at neck US
Yearly evaluation
• TSH, fT3, Tg and AbTg
• Neck US
• Imaging work-up (WBS, PET/CT)
• Surgery and/or 131I treatment

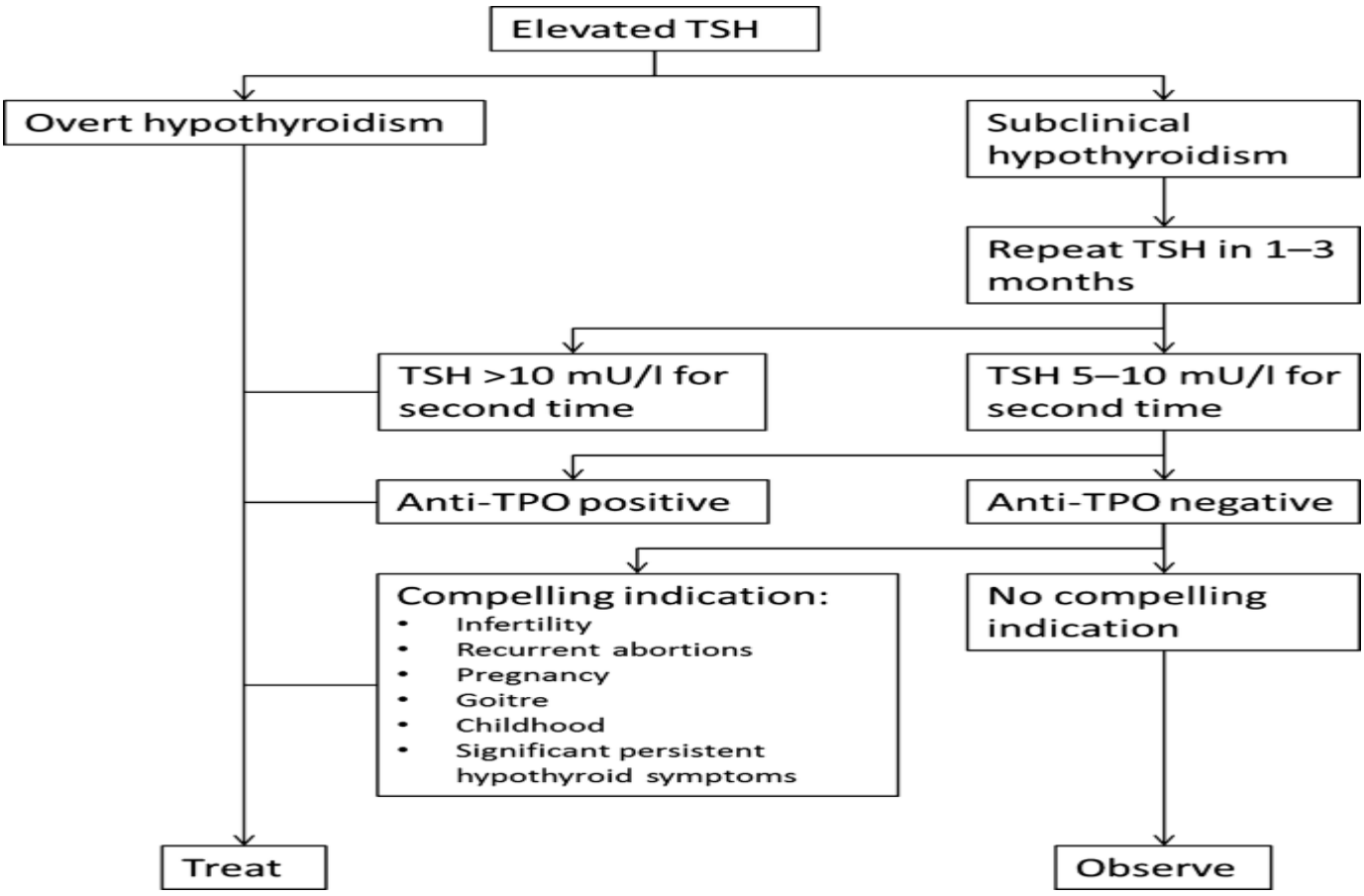
Thyroid disorders ; Management of Hypothyroidism



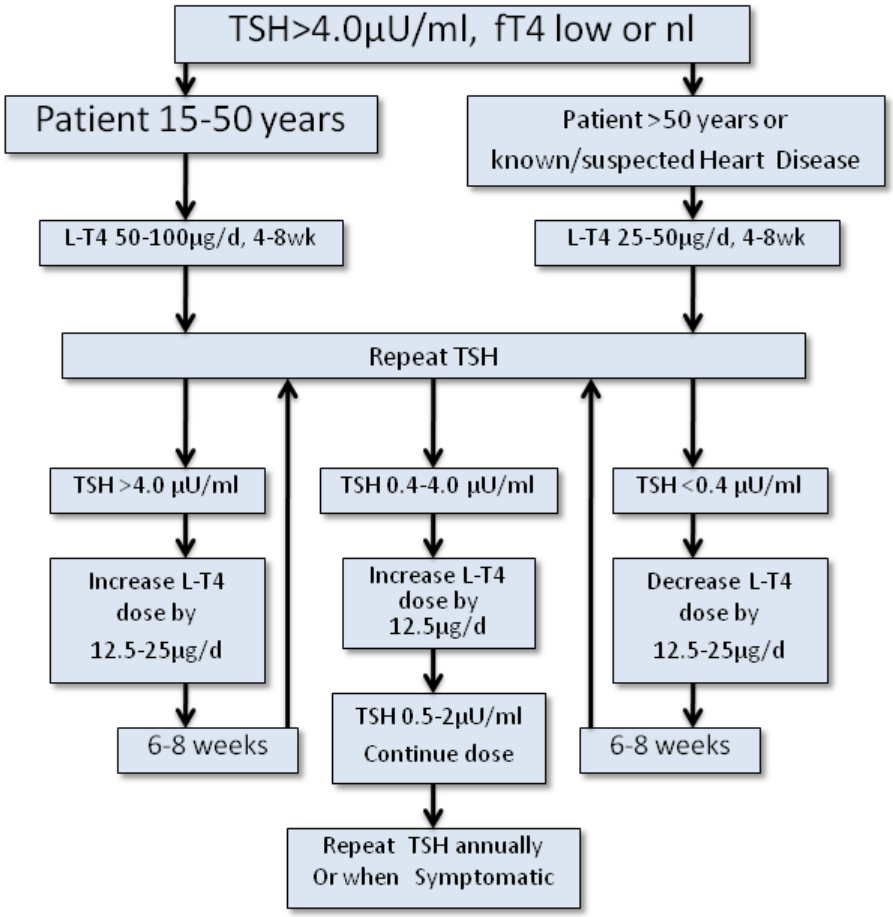
FT_4, free thyroxine; TSH, thyroid-stimulating hormone.



* In patients over 65 years of age, this algorithm should be applied on an individual basis.



Managing Primary Hypothyroidism

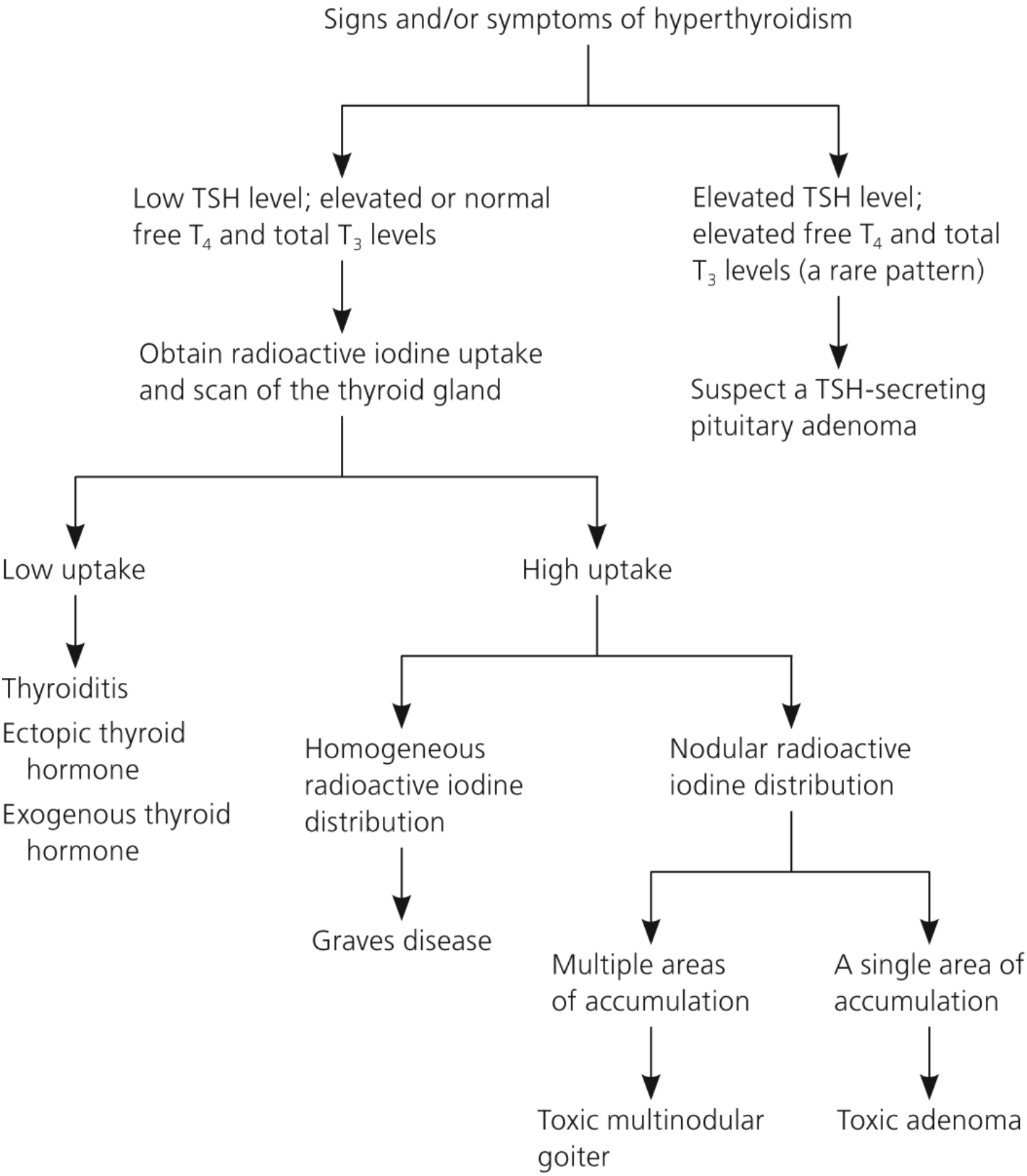


Conditions Requiring Special Attention:

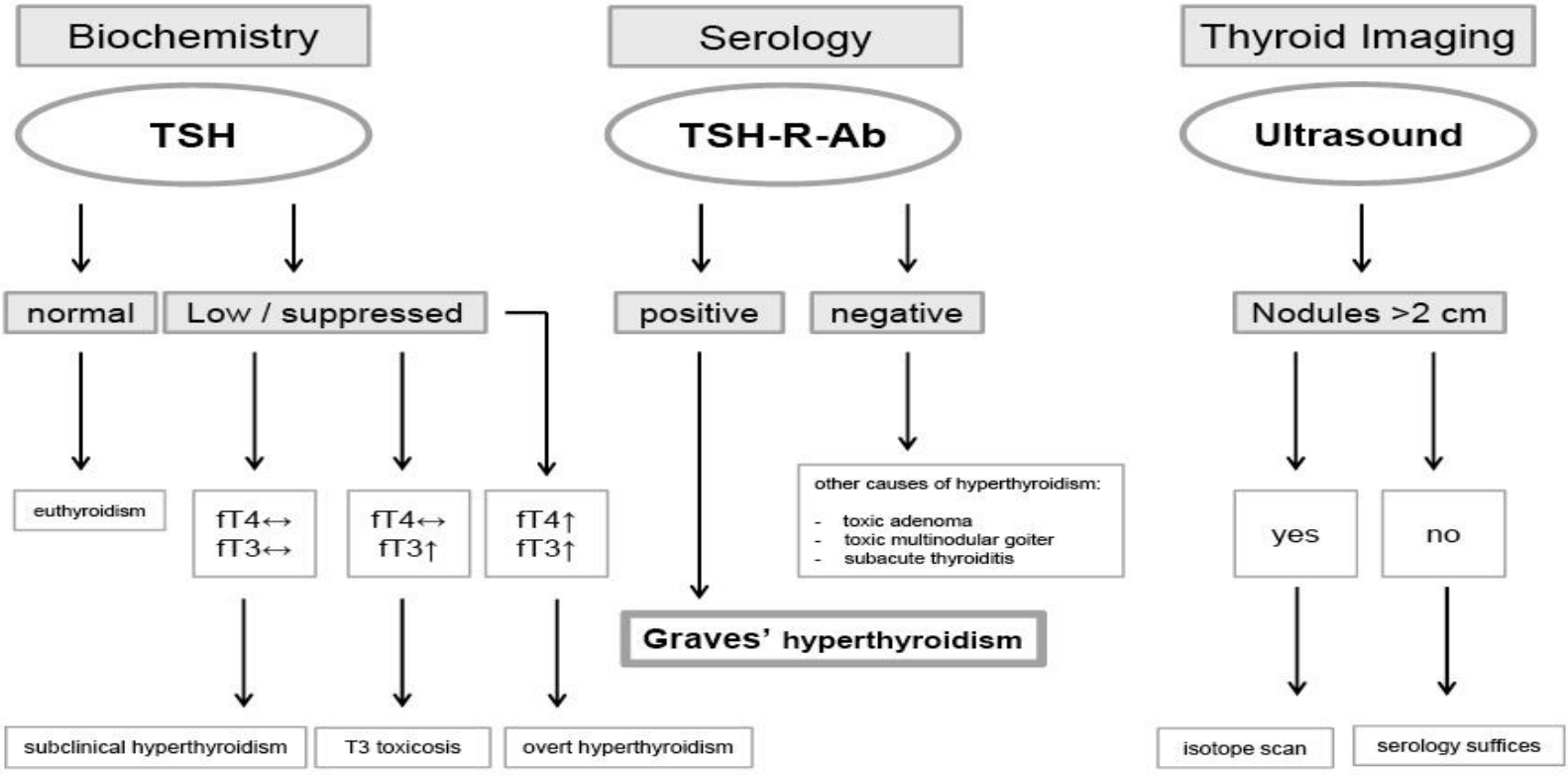
1. Cardiac compromised
2. Stupor; coma
3. Amiodarone treatment
4. Pre-op patient
5. ICU/CCU patient
6. Age<15 years
7. Sodium<130mEq/l
8. Pregnancy
9. Postpartum thyrotoxicosis
10. TSH persistently high or nonresponsive to T4
11. Symptoms of pituitary disease
12. Non-suppressible function in Hashimoto's or Graves'
13. Remember GRTH and PRTH

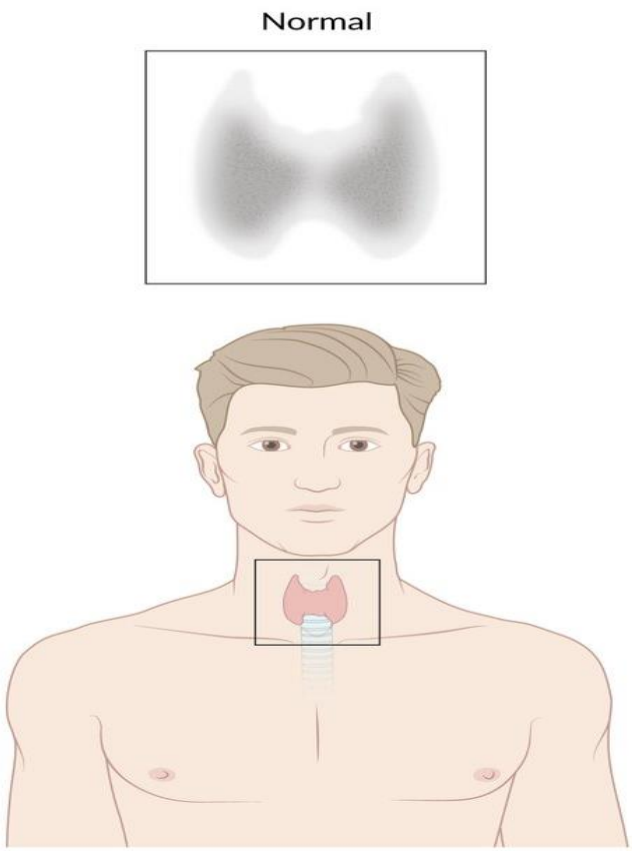
See also:
Correct Thyroxine Dosage Algorithm

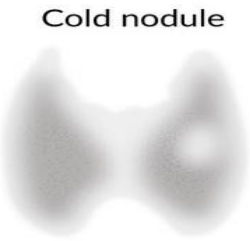
Thyroid disorders; Management of Hyperthyroidism

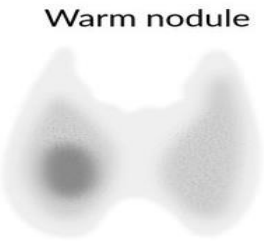

Signs and/or symptoms of hyperthyroidism
Low TSH level; elevated or normal free T_4 and total T_3 levels
Elevated TSH level; elevated free T_4 and total T_3 levels (a rare pattern)
Obtain radioactive iodine uptake and scan of the thyroid gland
Suspect a TSH-secreting pituitary adenoma
Low uptake
High uptake
Thyroiditis
Ectopic thyroid hormone
Exogenous thyroid hormone
Homogeneous radioactive iodine distribution
Nodular radioactive iodine distribution
Graves disease
Multiple areas of accumulation
A single area of accumulation
Toxic multinodular goiter
Toxic adenoma

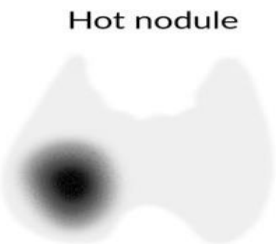
Thyroid disorders ; Management of Hyperthyroidism

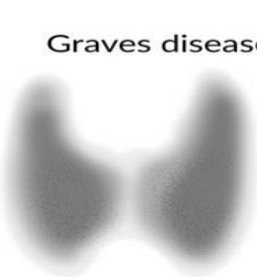


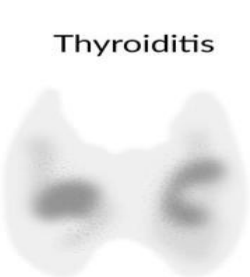


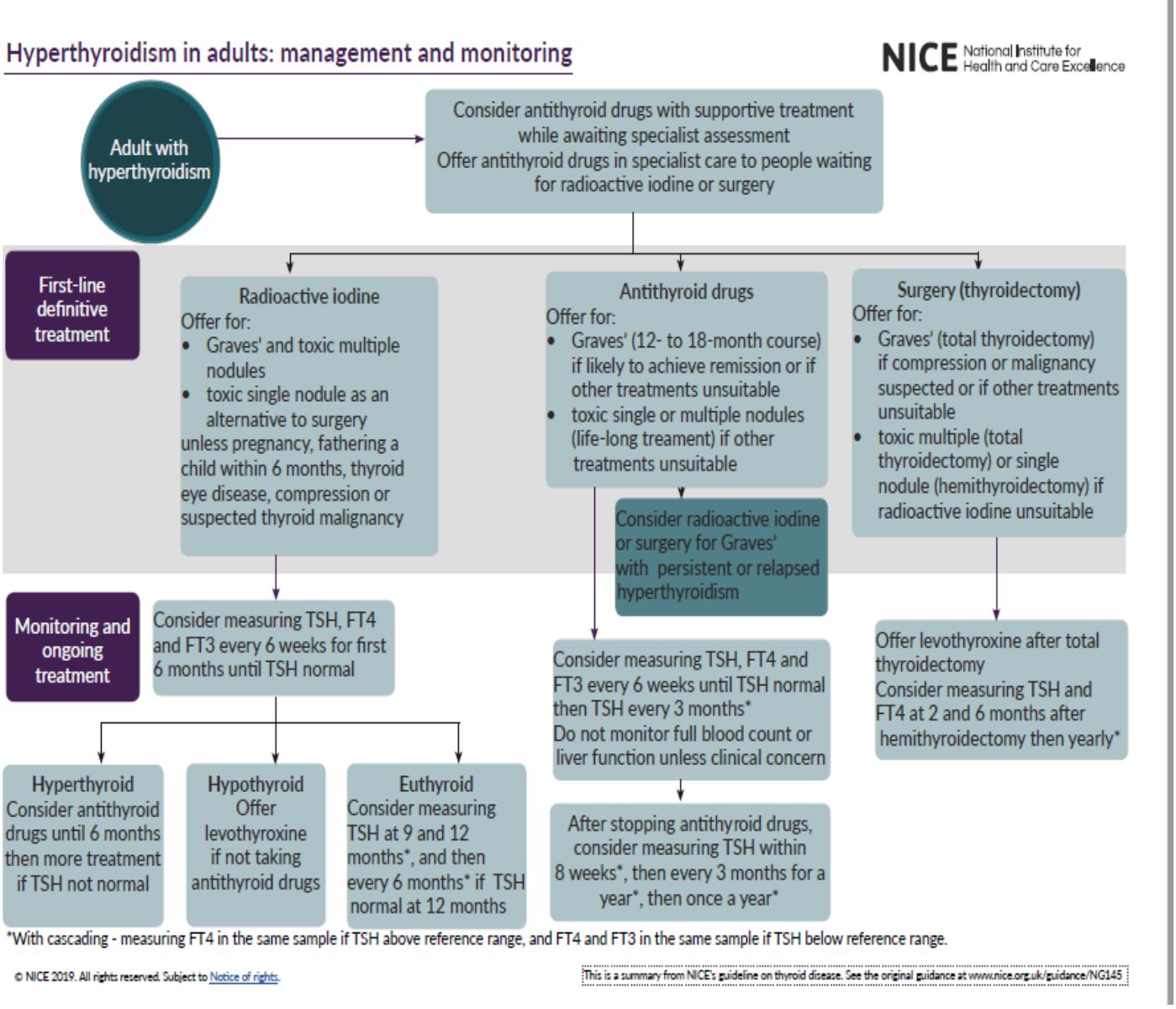


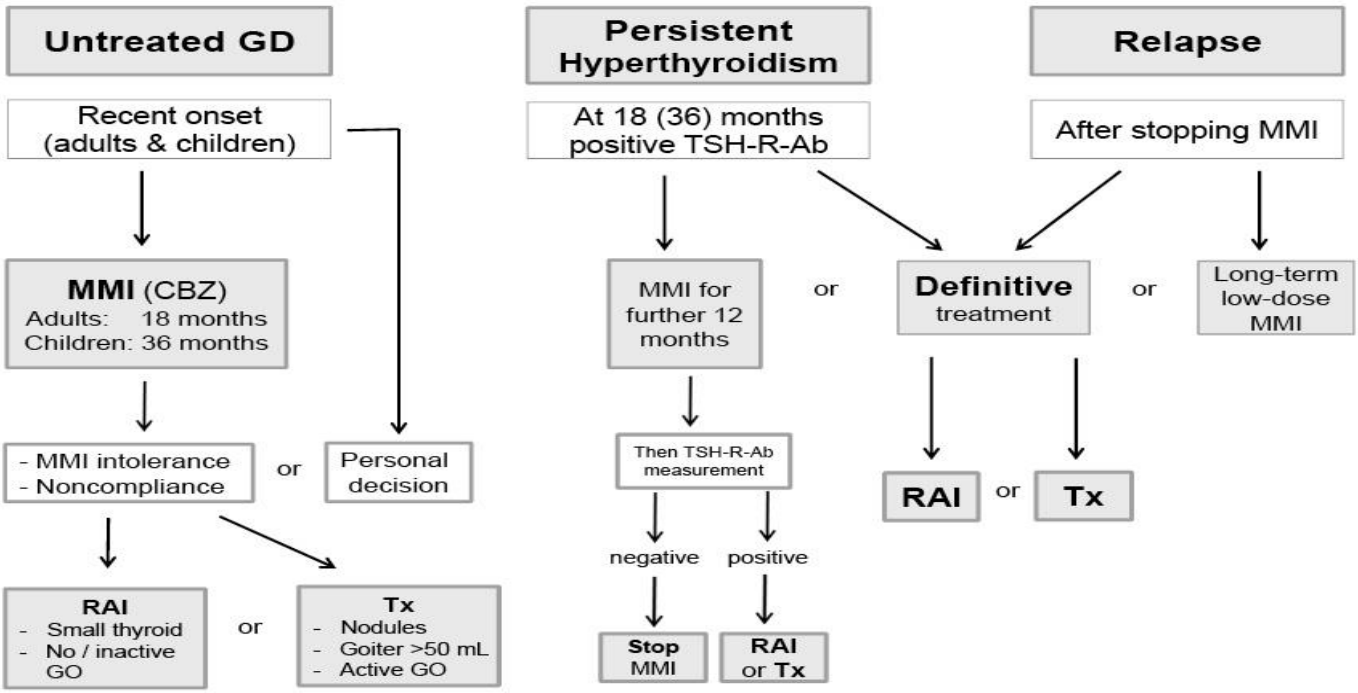




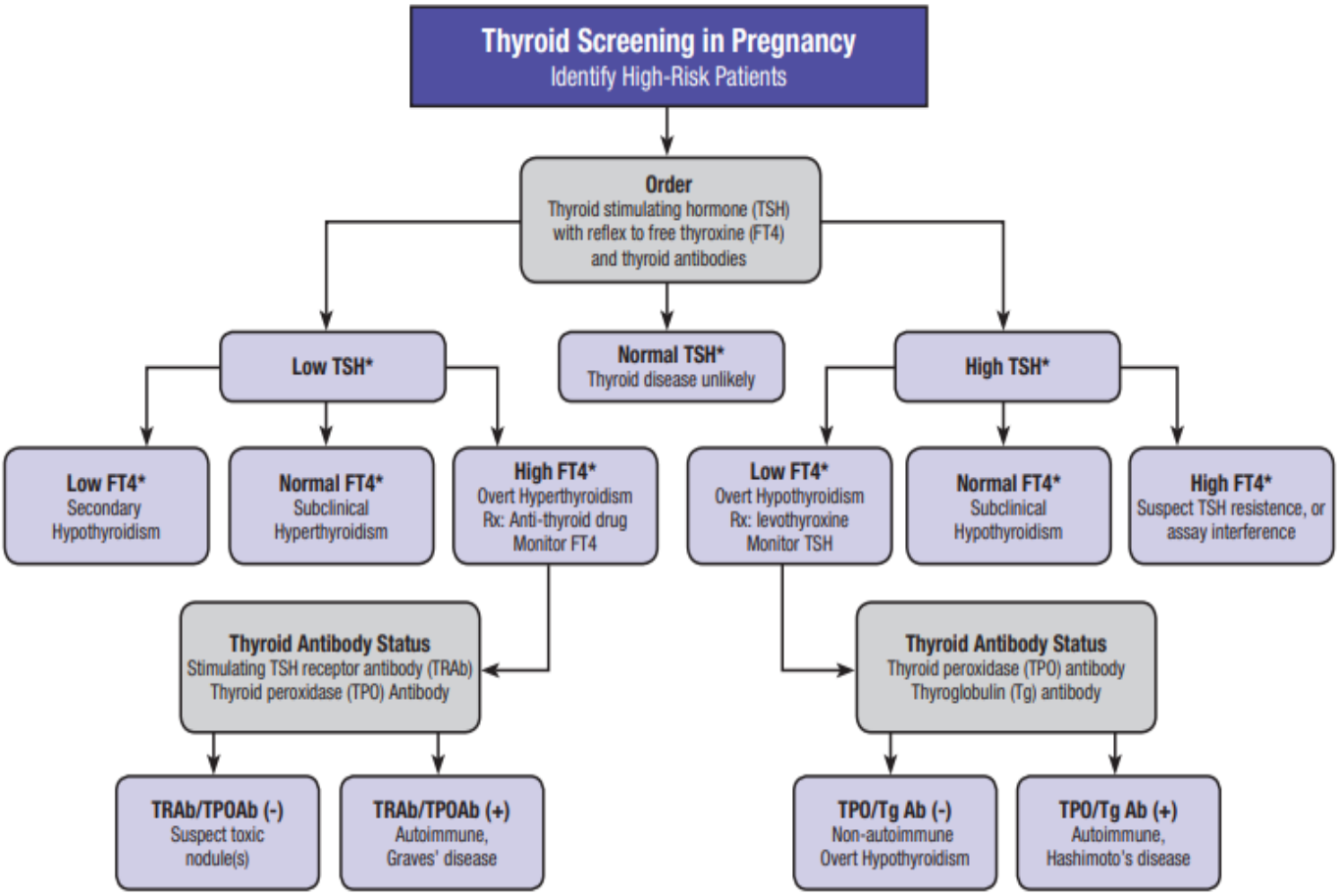





Hyperthyroidism in adults: management and monitoring
NICE National Institute for Health and Care Excellence
Adult with hyperthyroidism
Consider antithyroid drugs with supportive treatment while awaiting specialist assessment
Offer antithyroid drugs in specialist care to people waiting for radioactive iodine or surgery
First-line definitive treatment
Radioactive iodine
Offer for:
• Graves' and toxic multiple nodules
• toxic single nodule as an alternative to surgery
unless pregnancy, fathering a child within 6 months, thyroid eye disease, compression or suspected thyroid malignancy
Antithyroid drugs
Offer for:
• Graves' (12- to 18-month course) if likely to achieve remission or if other treatments unsuitable
• toxic single or multiple nodules (life-long treament) if other treatments unsuitable
Surgery (thyroidectomy)
Offer for:
• Graves' (total thyroidectomy) if compression or malignancy suspected or if other treatments unsuitable
• toxic multiple (total thyroidectomy) or single nodule (hemithyroidectomy) if radioactive iodine unsuitable
Consider radioactive iodine or surgery for Graves' with persistent or relapsed hyperthyroidism
Monitoring and ongoing treatment
Consider measuring TSH, FT4 and FT3 every 6 weeks for first 6 months until TSH normal
Consider measuring TSH, FT4 and FT3 every 6 weeks until TSH normal then TSH every 3 months*
Do not monitor full blood count or liver function unless clinical concern
Offer levothyroxine after total thyroidectomy
Consider measuring TSH and FT4 at 2 and 6 months after hemithyroidectomy then yearly*
Hyperthyroid
Consider antithyroid drugs until 6 months then more treatment if TSH not normal
Hypothyroid
Offer levothyroxine if not taking antithyroid drugs
Euthyroid
Consider measuring TSH at 9 and 12 months*, and then every 6 months* if TSH normal at 12 months
After stopping antithyroid drugs, consider measuring TSH within 8 weeks*, then every 3 months for a year*, then once a year*
*With cascading - measuring FT4 in the same sample if TSH above reference range, and FT4 and FT3 in the same sample if TSH below reference range.
© NICE 2019. All rights reserved. Subject to Notice of rights.
This is a summary from NICE's guideline on thyroid disease. See the original guidance at www.nice.org.uk/guidance/NG145

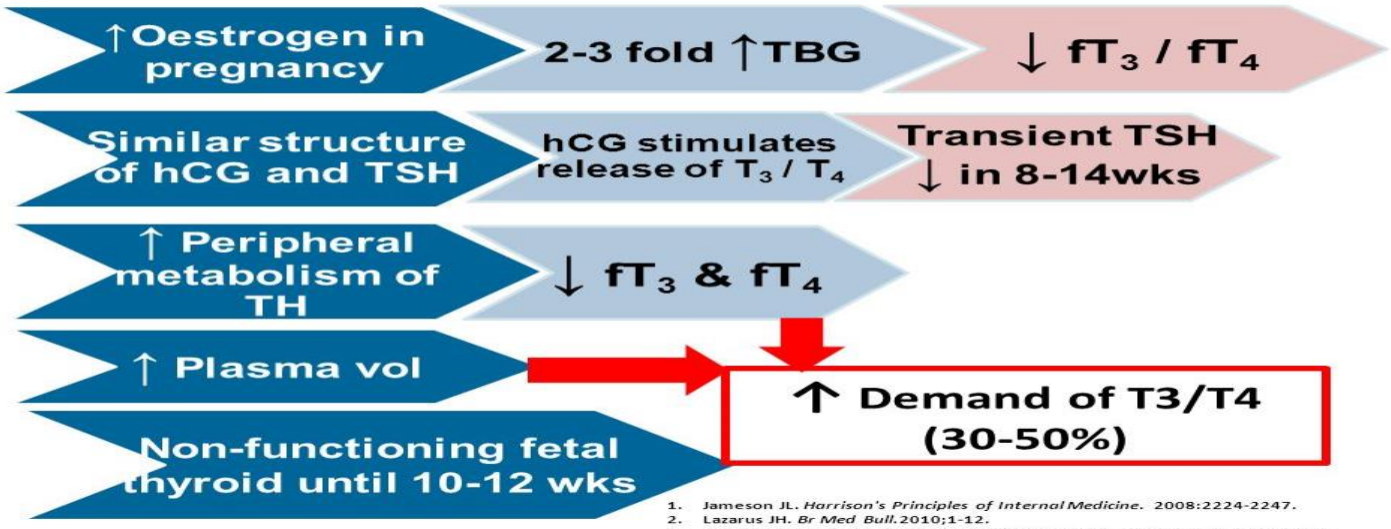

Untreated GD
Recent onset (adults & children)
MMI (CBZ)
Adults: 18 months
Children: 36 months
- MMI intolerance
- Noncompliance
or
Personal decision
RAI
- Small thyroid
- No / inactive GO
or
Tx
- Nodules
- Goiter >50 mL
- Active GO
Persistent Hyperthyroidism
At 18 (36) months positive TSH-R-Ab
MMI for further 12 months
Then TSH-R-Ab measurement
negative
positive
Stop MMI
RAI or Tx
or
Definitive treatment
RAI
or
Tx
Relapse
After stopping MMI
or
Long-term low-dose MMI

F2 Diagnostic Algorithm for Assessing Thyroid Function in Pregnancy



Diagnostic testing algorithm for assessing thyroid function in pregnancy. High-risk patients include: personal or family history of thyroid disease, clinical signs and/or symptoms of thyroid disease, presence of goiter on physical exam, >30 years age, high body mass index, type 1 diabetes or presence of other autoimmune disorders, thyroid peroxidase antibody positive, previous head or neck irradiation, history of preterm birth, miscarriage, infertility, patient from iodine deficient region. (*) Determined utilizing assay and trimester specific reference ranges representative of the patient population

Thyroid Physiology in Pregnancy

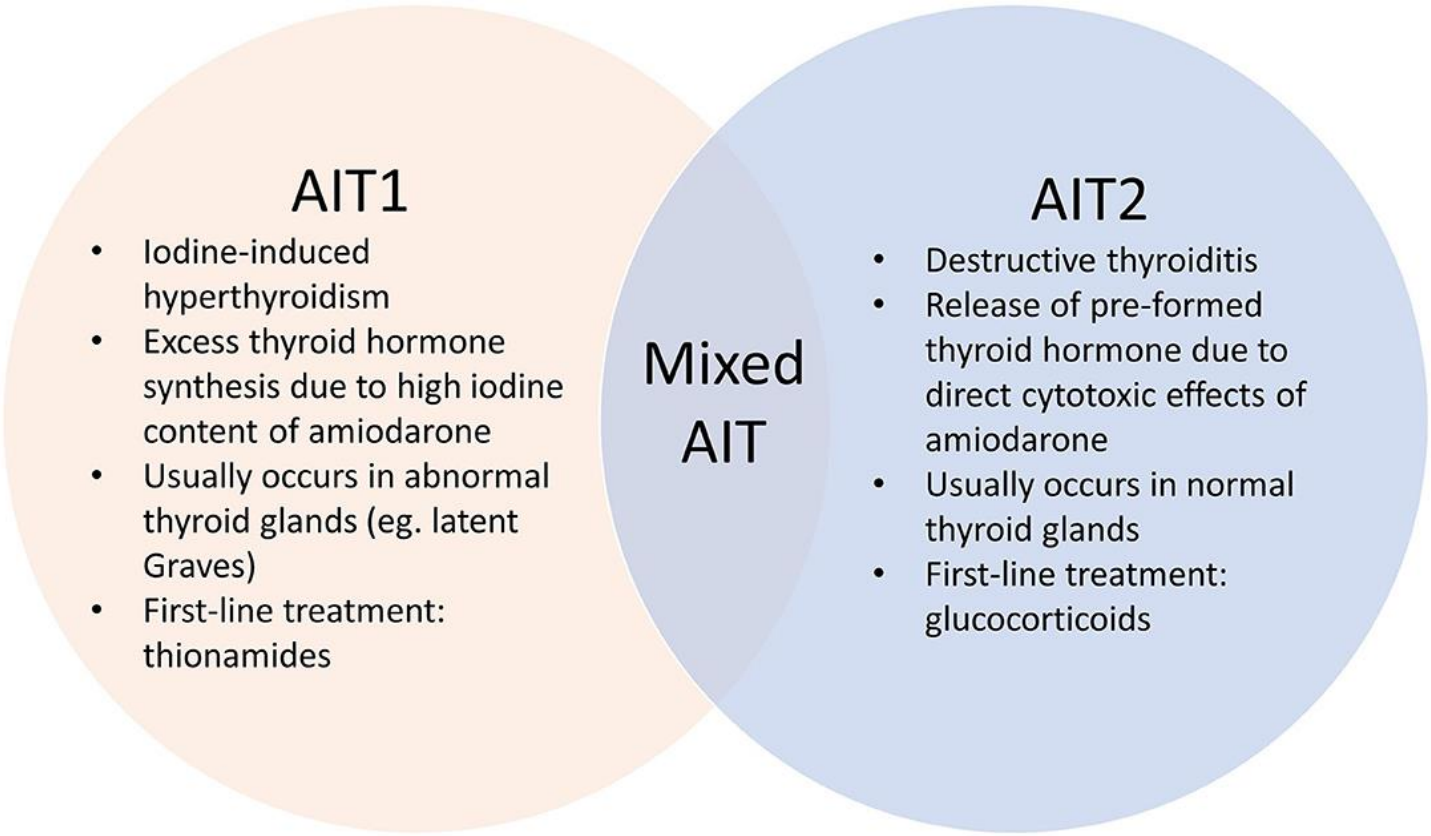

↑Oestrogen in pregnancy
2-3 fold ↑TBG
↓ fT3 / fT4
Similar structure of hCG and TSH
hCG stimulates release of T3 / T4
Transient TSH ↓ in 8-14wks
↑ Peripheral metabolism of TH
↓ fT3 & fT4
↑ Plasma vol
↑ Demand of T3/T4 (30-50%)
Non-functioning fetal thyroid until 10-12 wks

1. Jameson JL. *Harrison's Principles of Internal Medicine*. 2008:2224-2247.
2. Lazarus JH. *Br Med Bull*.2010;1-12.
3. Galofre JC, Davies TF. *J Womens Health (Larchmt)*. 2009;18(11):1847-1856..

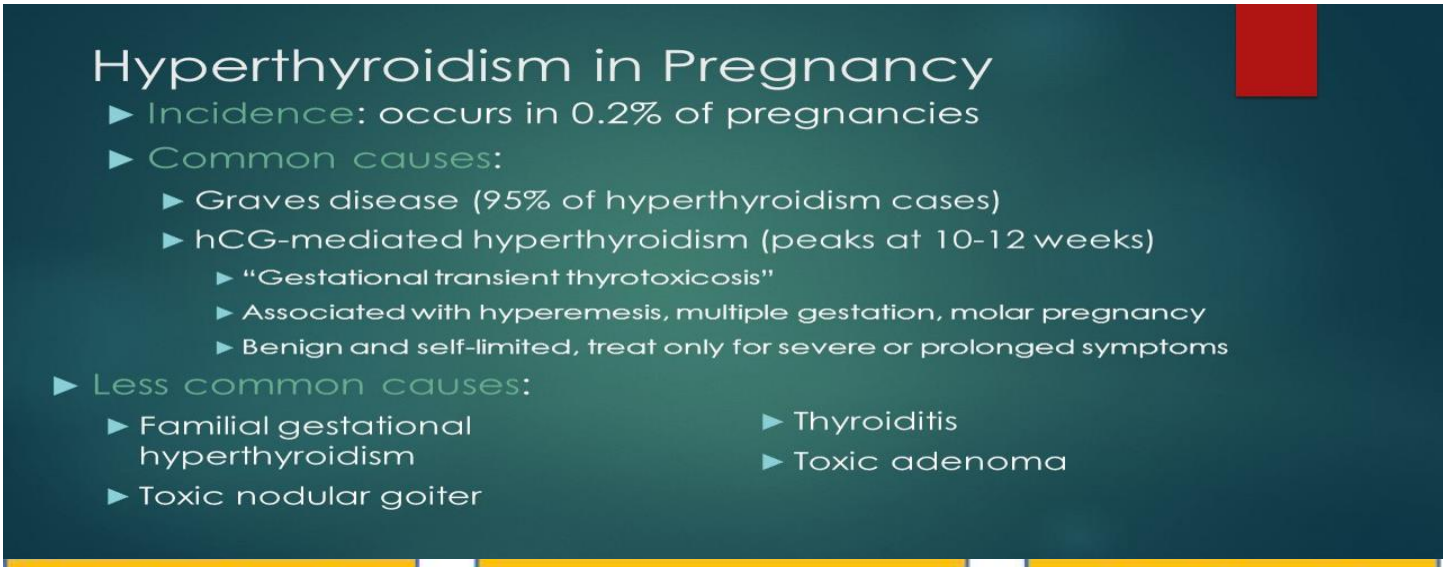
Table 1.5 Atypical thyroid function tests

Test	Possible cause
Suppressed TSH and normal FT_4	T_3 toxicosis (~5% of thyrotoxicosis)
Suppressed TSH and normal FT_4 and free T_3 (FT_3)	Subclinical hyperthyroidism Recovery from thyrotoxicosis Excess thyroxine replacement NTI
Detectable TSH and elevated FT_4 and FT_3	TSH-secreting pituitary tumour Thyroid hormone resistance Heterophile antibodies, leading to spurious measurements of FT_4 and FT_3 Thyroxine replacement therapy (including poor compliance)
Elevated FT_4 and FT_3, and suppressed TSH	Biotin
Elevated FT_4 and low-normal FT_3, normal TSH	Amiodarone
Elevated free T_4 and T_3	Heparin
Suppressed or normal TSH, and low-normal FT_4 and FT_3	NTI Central hypothyroidism Isolated TSH deficiency

Remember !!! . Amiodarone Thyroid effect


AIT1
Iodine-induced hyperthyroidism
Excess thyroid hormone synthesis due to high iodine content of amiodarone
Usually occurs in abnormal thyroid glands (eg. latent Graves)
First-line treatment: thionamides
Mixed AIT
AIT2
Destructive thyroiditis
Release of pre-formed thyroid hormone due to direct cytotoxic effects of amiodarone
Usually occurs in normal thyroid glands
First-line treatment: glucocorticoids

Thyroid disorders; thyroid dysfunction in pregnancy


Hyperthyroidism in Pregnancy
► Incidence: occurs in 0.2% of pregnancies
► Common causes:
► Graves disease (95% of hyperthyroidism cases)
► hCG-mediated hyperthyroidism (peaks at 10-12 weeks)
► "Gestational transient thyrotoxicosis"
► Associated with hyperemesis, multiple gestation, molar pregnancy
► Benign and self-limited, treat only for severe or prolonged symptoms
► Less common causes:
► Familial gestational hyperthyroidism
► Toxic nodular goiter
► Thyroiditis
► Toxic adenoma

Gestational transient thyrotoxicosis	Graves ' disease	Toxic thyroid nodule
•Low TSH elevated T3, mildly elevated or normal T4	•Low TSH, elevated T4, normal or mildly elevated T3	•Low TSH elevated T3, mildly elevated or normal T4
•TRab negative	•TRab positive	•TRab negative
•No goitre	•Difuse goitre	•Solitary or multinodular goitre
•T3/T4 ratio <20	•T3/T4 ratio > 20	

Gestational thyrotoxicosis (GTT) with or without hyperemesis gravidarum is described as non immune, self limited , hCG-mediated hyperthyroidism that occurs in the first trimester of pregnancy; it is generally asymptomatic with mild biochemical hyperthyroidism.

Distinguishing true overt hyperthyroidism from GTT in a setting of hyperemesis gravidarum is challenging. The absence of clinical signs of hyperthyroidism and negative thyroid antibodies supports the diagnosis of GTT.

Remember !!! thyroid sacn is contraindicated in Pregnancy

Adrenal disorders, management of secondary Hypertension

Secondary hypertension need to consider screening tests. These include (1) resistant hypertension, (2) abrupt onset of hypertension, (3) onset at an age less than 30 years, (3) disproportionate end-organ damage for the degree of hypertension, (4) accelerated or malignant hypertension, (5) onset of diastolic hypertension in a patient older than 65 years, and (6) unprovoked hypokalemia.

Resistant hypertension is uncontrolled blood pressure despite the use of 3 antihypertensive medications (one of which must be a diuretic)

Table 1. Some Causes of Secondary Hypertension With Associated Clinical Clues

Cause of Secondary Hypertension	Clinical Clues
Obstructive sleep apnea	Nocturnal gasping, morning headache, reported apnea, excessive daytime sleepiness, snoring.[12]
Renal artery stenosis	Worsening difficulty with hypertension control. Hypertensive crisis with flash pulmonary edema. Early-onset hypertension in young woman (fibromuscular dysplasia). Abdominal continuous bruit (systolic and diastolic).[10]
Renal parenchymal disease	Elevated serum creatinine level. Abnormal urinalysis findings.
Primary aldosteronism	Hypertension with spontaneous or diuretic-inducted hypokalemia. Hypertension with adrenal incidentaloma.[13]
Pheochromocytoma	Hypertension with autonomic disturbances, panic attacks, or adrenal incidentaloma. Familial disease with predisposition to pheochromocytoma.[14]
Cushing syndrome	Unusual age-related features of hypertension or osteoporosis in young adult. Treatment-resistant hypertension or osteoporosis. Proximal weakness or wide purple striae.[15]
Aortic coarctation	Elevated blood pressure measurement in arms with diminished or absent femoral artery pulses.[16]
Hyperthyroidism/ hypothyroidism	Heat or cold intolerance, fatigue, tremor, palpitations, weight change, diaphoresis, hair or skin changes.
Hyperparathyroidism	Bone pain, muscle weakness, nephrolithiasis, fatigue, confusion, anorexia.

Blood Pressure Categories

American Heart Association | American Stroke Association

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

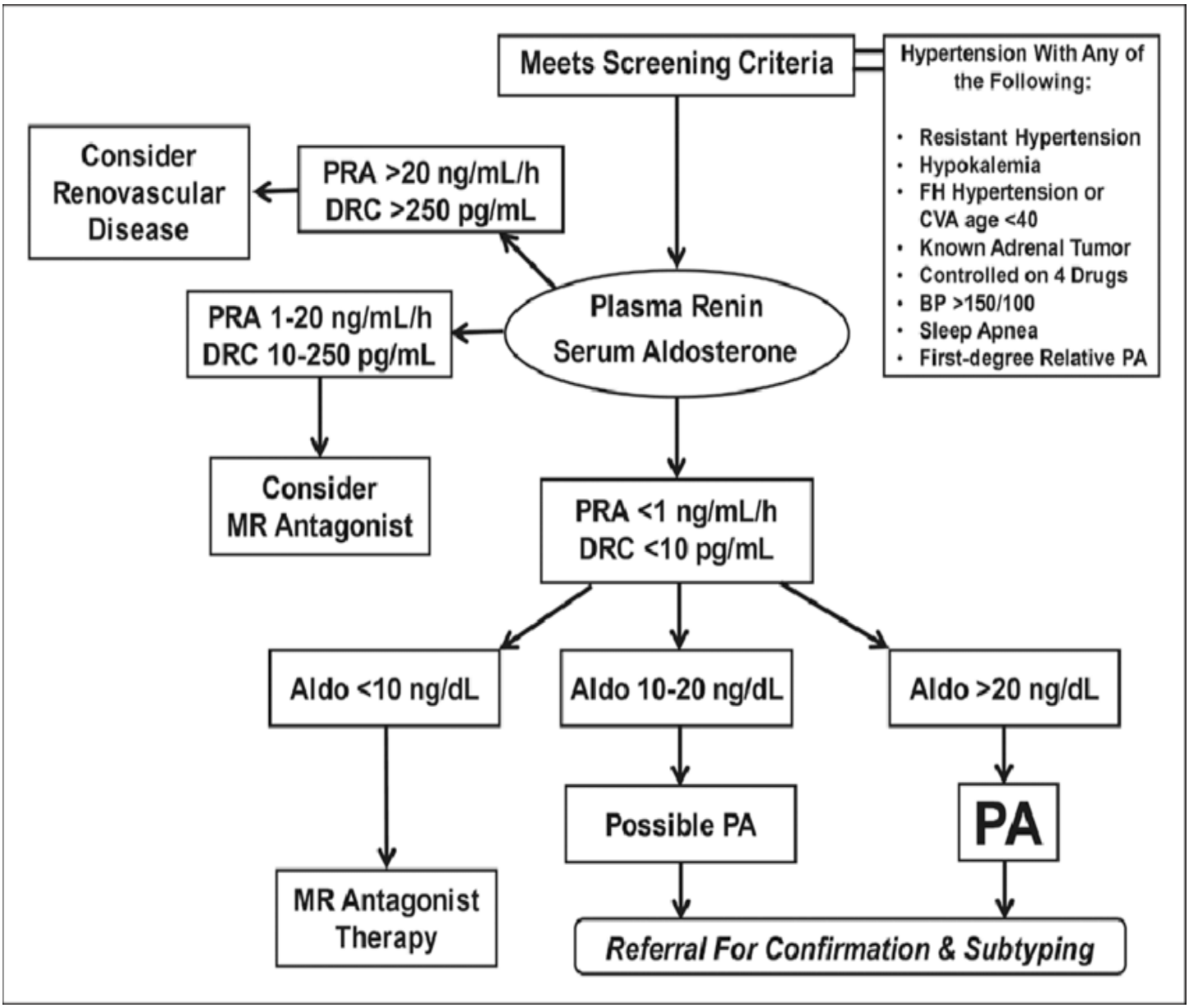
©American Heart Association

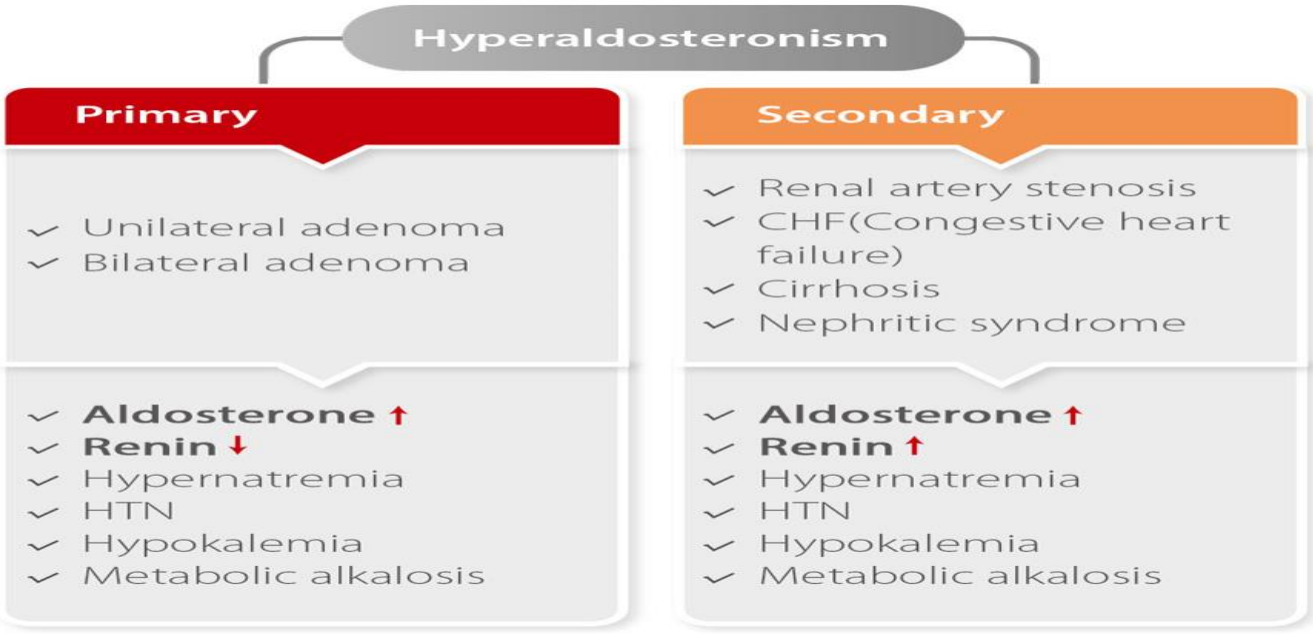
heart.org/bplevels

Table 2. Summary of Indications to Screen and Diagnostic Approach for Specific Causes of Secondary Hypertension

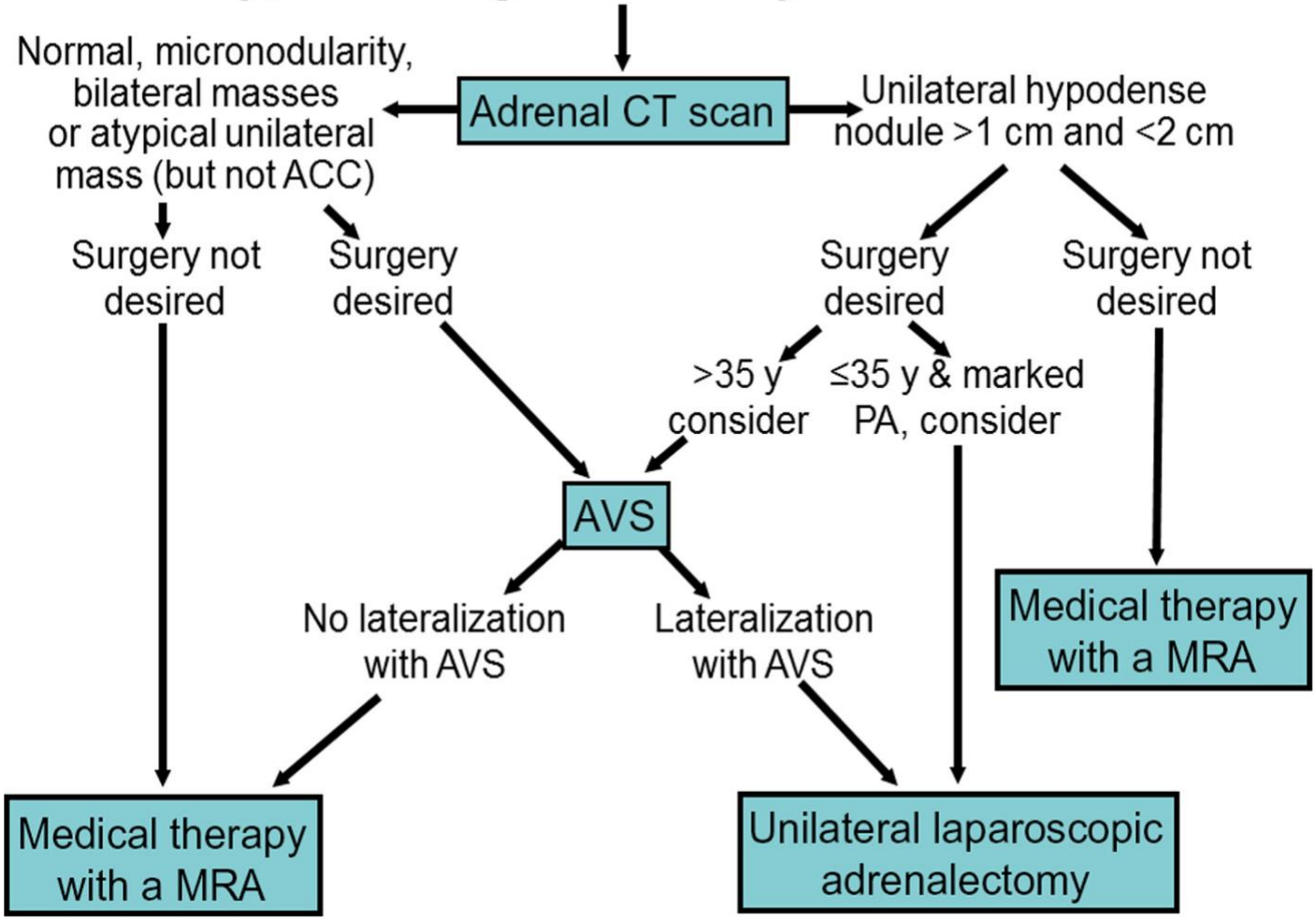
Cause of Secondary Hypertension	Indications to Screen	Diagnostic Approach
Obstructive sleep apnea	Likely at high risk of moderate to severe obstructive sleep apnea by combination of excessive daytime fatigue with at least 2 of 3 additional findings of (1) habitual loud snoring (2) witnessed apnea, gasping or choking, or (3) diagnosed hypertension.[17]	Sleep study.
Renal artery stenosis	Treatment-resistant hypertension with abnormal renal function or young adult with suspected fibromuscular dysplasia.	Duplex ultrasonography, magnetic resonance angiography, or computed tomography angiography.[18]
Renal parenchymal disease	Abnormal renal function or urinalysis findings.	Renal ultrasonography, urinalysis, metabolic panel.
Primary aldosteronism	(1) Sustained pressures greater than 150/100 mm Hg, (2) treatment-resistant hypertension, (3) hypertension with spontaneous or diuretic-induced hypokalemia, (4) hypertension with the presence of an adrenal incidentaloma, (5) hypertension with a family history of early-onset hypertension, stroke at a young age, or a first-degree family history of primary aldosteronism.[13]	Screen with plasma aldosterone concentration to plasma-renin activity ratio. Confirmatory testing, if indicated, with oral sodium loading test, saline infusion test, fludrocortisone suppression test, or a captopril challenge.[13]
Pheochromocytoma	Treatment-resistant hypertension and/or suggestive symptoms/signs.	Plasma free-metanephrines test (if available) or plasma catecholamines and 24-hour urine fractioned metanephrines test.[19]
Cushing syndrome	Treatment-resistant hypertension and/or suggestive symptoms/signs.	Exclude exogenous glucocorticoids then any 2 of (1) late-night salivary cortisol, (2) 24-hour urine free cortisol, or (3) dexamethasone suppression with a 1-mg overnight or a 2-mg 2-day test.[15]
Aortic coarctation	Treatment-resistant hypertension and/or suggestive symptoms/signs.	Transthoracic echocardiography.
Hyperthyroidism/hypothyroidism	Suggestive symptoms/signs.	Thyrotropin, free thyroxine, triiodothyronine tests.
Hyperparathyroidism	Suggestive symptoms/signs.	Serum calcium, parathyroid hormone tests.

Adrenal disorders. Management of Primary hyperaldosteronism

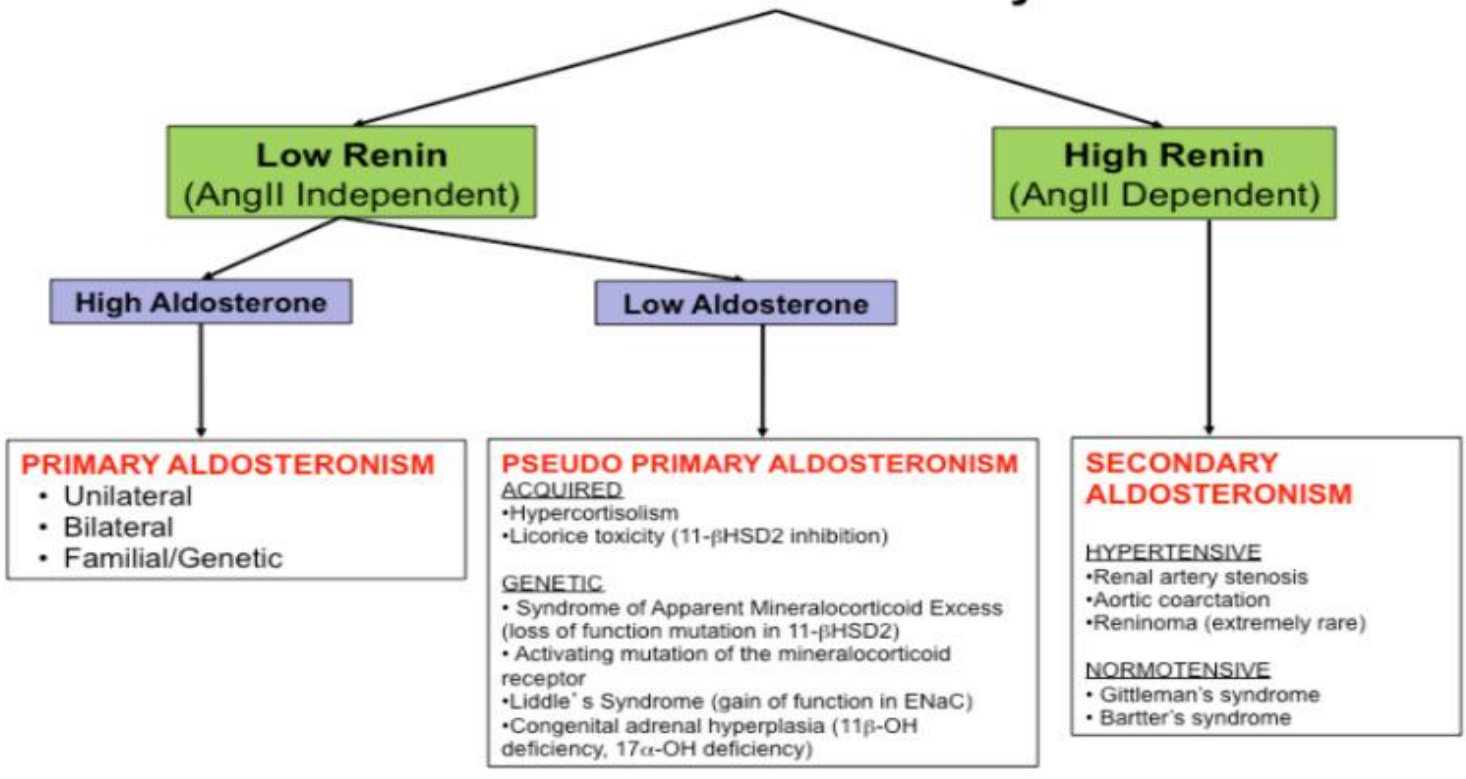




Subtype Testing for Primary Aldosteronism



Mineralocorticoid Excess Syndrome



Adrenal disorders. Management of Adrenal mass

Incidental Adrenal Mass (>1 cm) diagnosed on CT/MRI
Hormonal evaluation in all patients
1. Dexamethasone (1 mg) suppression test
2. Plasma or 24-h urine metanephrines
3. If hypertensive, include plasma aldosterone:renin ratio

Functional Mass
(Hormonal evaluation abnormal/positive)

Endocrinology Consultation
- Confirmation testing of autonomous secretion of cortisol, catecholamines, aldosterone, other
- Medical and preoperative management

Consider surgery

Positive autonomous hormonal secretion
Growth >1 cm
Size of mass ≥ 4 cm

Nonfunctional Mass
(Hormonal evaluation normal/negative)

Size of adrenal mass <4 cm

Benign Imaging Features
- Homogenous
- Low density
- Smooth margins
- Unenhanced CT ≤10-HU attenuation

Consider Conservative Management
- Repeat imaging 6–12 mo
- Repeat hormonal evaluation annually for 4 yr

Suspicious Imaging Features
- Heterogeneous
- Necrosis
- Irregular margins
- Unenhanced CT >10-HU attenuation

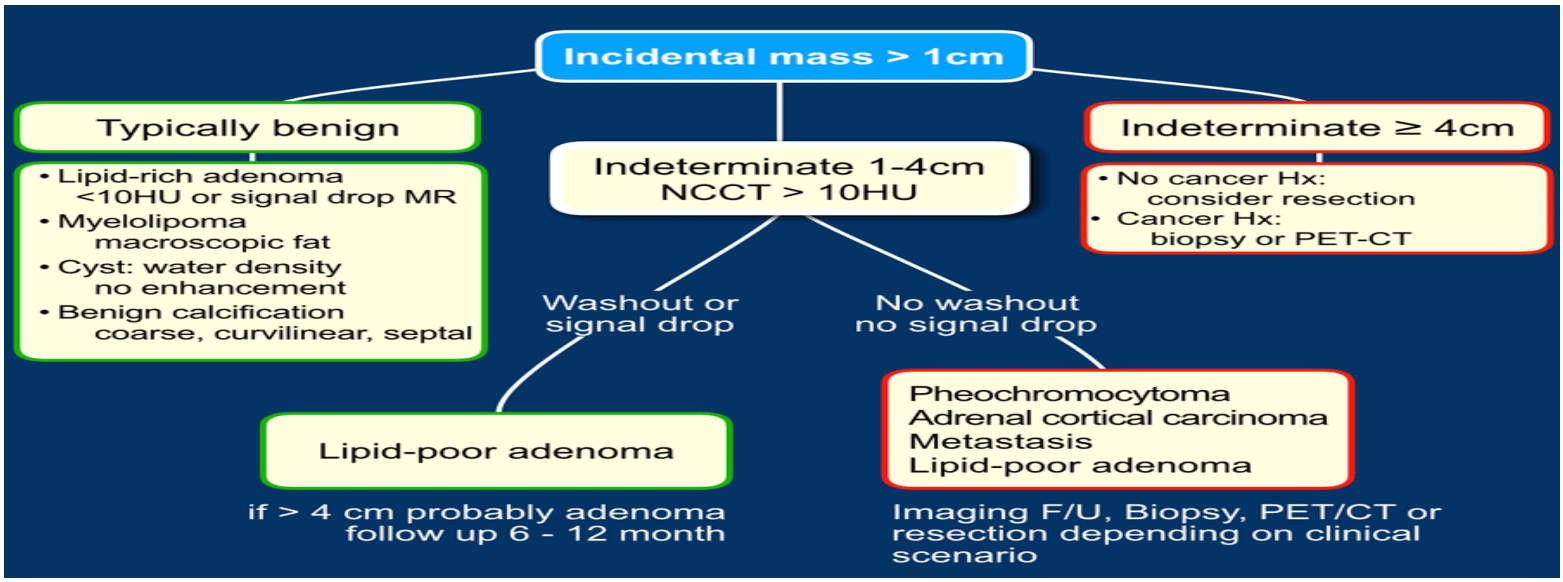
CT with contrast

≥50% contrast washout at 10 min

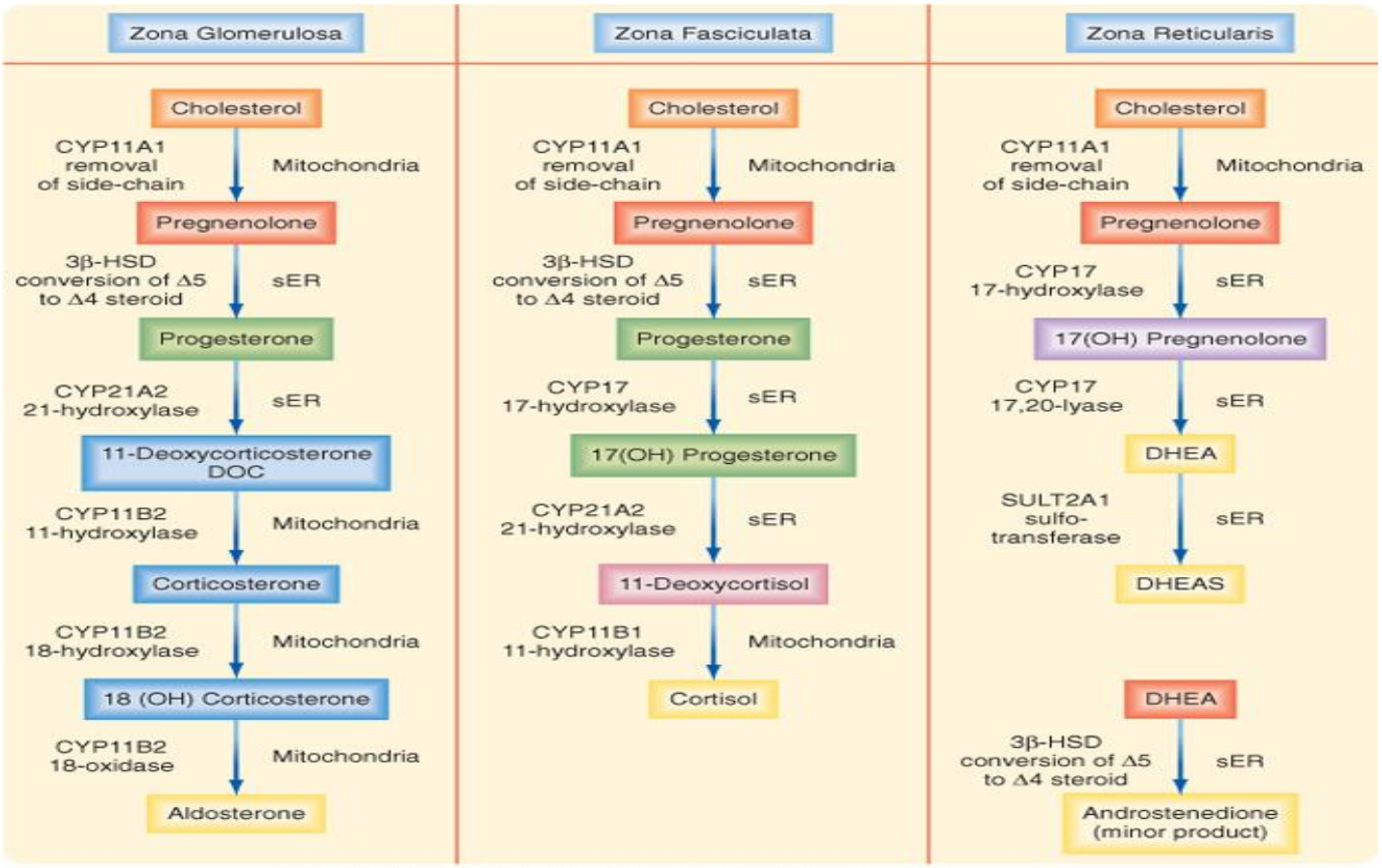
<50% contrast washout at 10 min

Size of adrenal mass ≥4 cm

Consider Surgery
- If history of malignancy: PET-CT, biopsy



Adrenal disorders. Management of Congenital Adrenal hyperplasia



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.
Copyright © 2008 by Mosby, an imprint of Elsevier, Inc. All rights reserved

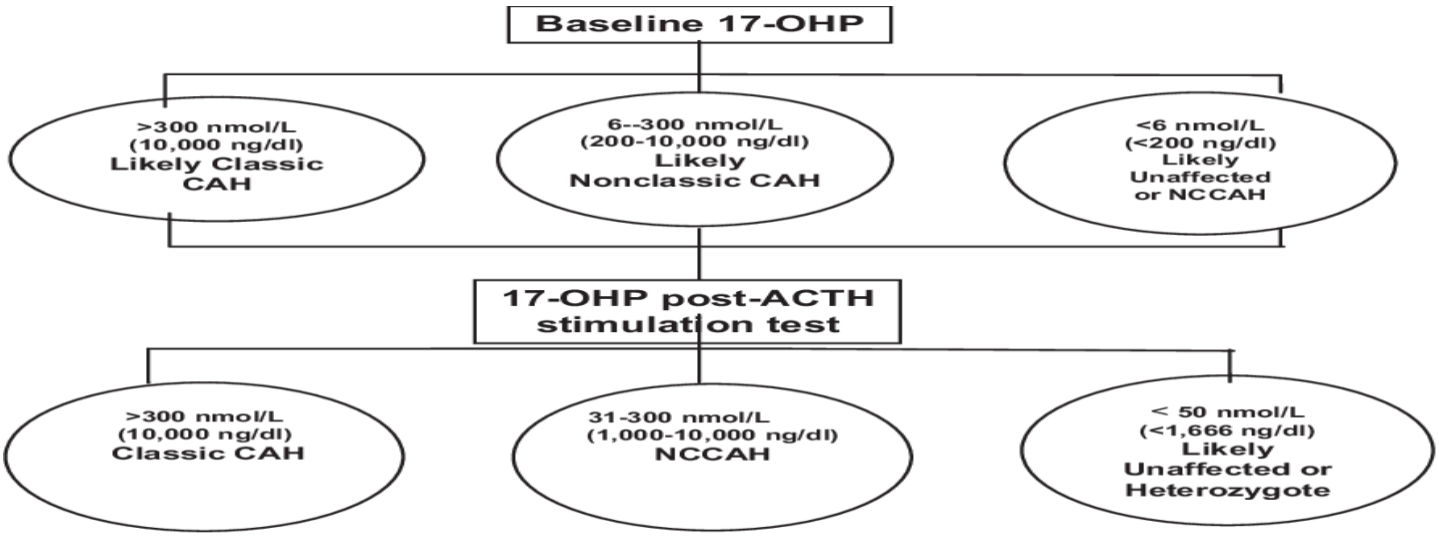


FIG. 2. Diagnosis of CAH after infancy. Reference standards for hormonal diagnosis derived

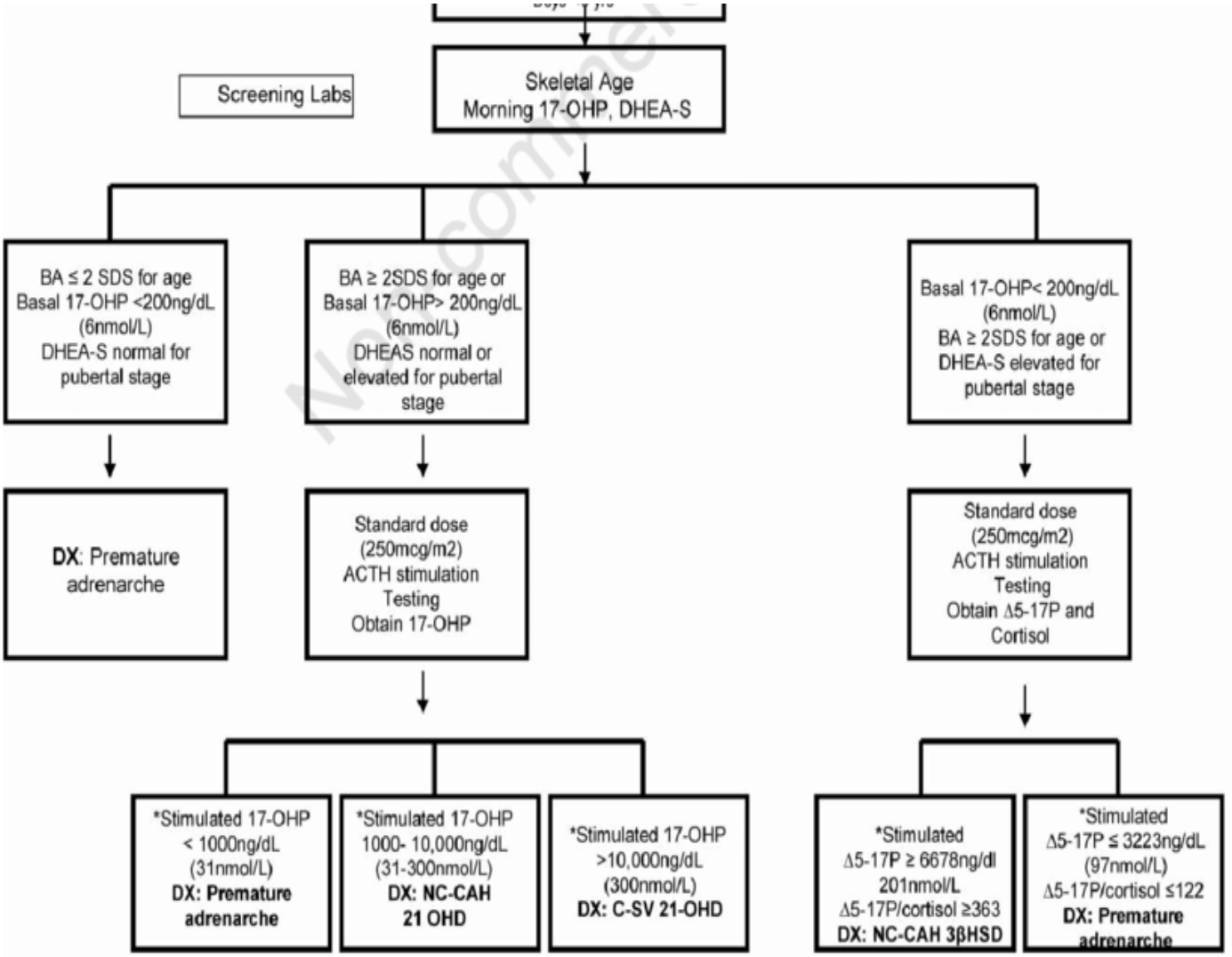
Adrenal disorders, management of congenital adrenal hyperplasia

Table 1. Diagnosis and Treatment of Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (CAH) According to Age.*

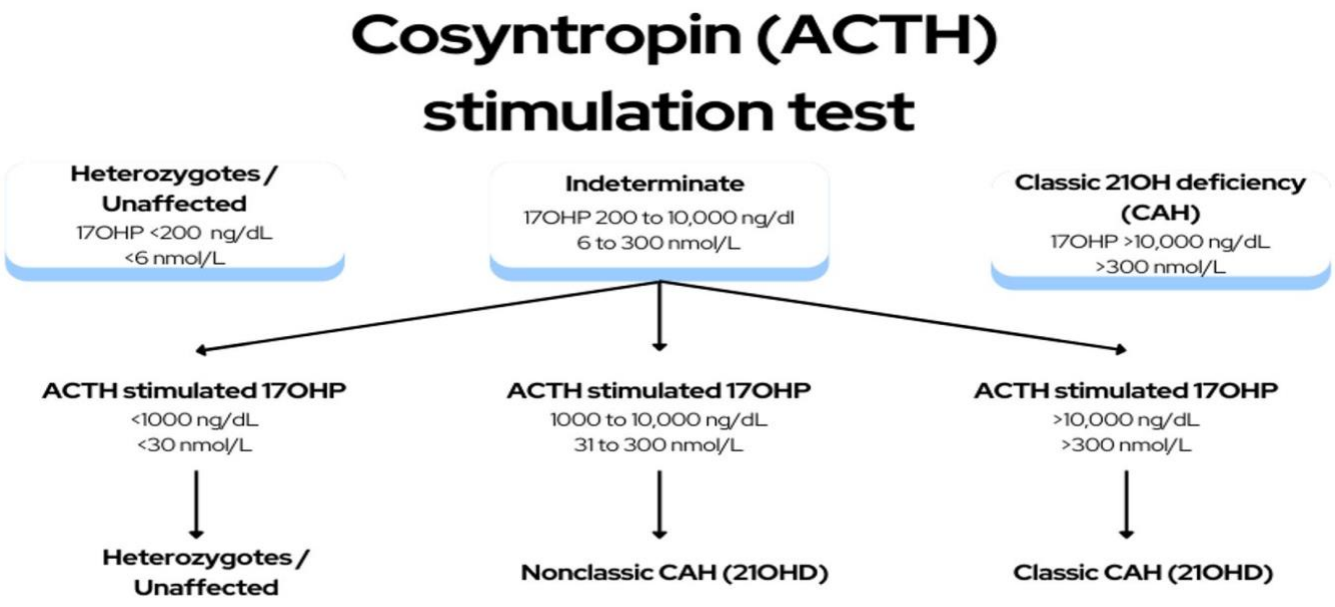
Approach	Infancy	Childhood	Adolescence and Adulthood
Diagnosis			
Symptoms and signs at presentation	Positive newborn screen, atypical genitalia (46,XX), poor feeding, weight loss, dehydration with low sodium, high potassium	Increased growth velocity, precocious pubarche†, early-onset adult apocrine odor	Hirsutism, oligomenorrhea, subfertility
Hormonal findings	Increased 17-OHP and androstenedione, decreased cortisol (in classic CAH) Corticotropin (cosyntropin) stimulation: 17-OHP >1000 ng/dl (30 nmol/liter), usually >5000 ng/dl (150 nmol/liter) in classic CAH Rule out other rare disorders of steroidogenesis‡	Same as for infancy	Corticotropin (cosyntropin) stimulation: 17-OHP >1000 ng/dl (30 nmol/liter) In nonclassic CAH, cortisol normal or near normal
Additional considerations	Pelvic ultrasonography to determine presence or absence of uterus in cases of atypical genitalia Measurement of electrolytes to evaluate sodium and potassium homeostasis Stimulation test may be delayed in sick infants	Radiographic assessment of bone age (left hand) to assess for skeletal maturation Distinguish classic from nonclassic CAH on the basis of cortisol values and disease severity	Early-morning, follicular-phase 17-OHP <200 ng/dl (6 nmol/liter) often rules out nonclassic CAH Genotyping and genetic counseling before pregnancy
Treatment			
At diagnosis	Treatment initiated after testing and before results are available, to prevent adrenal crisis	Treatment indicated for classic CAH and symptomatic nonclassic CAH	Treatment indicated for symptomatic nonclassic CAH
Long-term therapy	Hydrocortisone three times daily (10–18 mg/m^2/day) Fludrocortisone (50–200 μg) once or twice daily Sodium chloride, 1 to 2 g (17 to 34 mmol/liter) per day, divided into several feedings, in first year	Classic CAH: hydrocortisone three times daily (10–18 mg/m^2/day); fludrocortisone (50–200 μg) once or twice daily Nonclassic CAH: hydrocortisone three times daily (8–12 mg/m^2/day)	Classic CAH: may use hydrocortisone (approximately 15–40 mg/day), long-acting glucocorticoid§, or both; continue fludrocortisone Nonclassic CAH: hydrocortisone twice or three times daily, or prednisone or prednisolone, generally ≤4 mg/day
Stress dosing for prevention of adrenal crisis	For febrile illnesses, 2–3 times usual daily dose of glucocorticoid divided into 4 doses given every 6 hr Increased fluid intake and frequent ingestion of simple and complex carbohydrates Intramuscular injection of hydrocortisone, 50–100 mg/m^2, if oral intake not possible; activate emergency services after injection	For febrile illnesses, 2–3 times usual daily dose of glucocorticoid, divided into 4 doses given every 6 hr Increased fluid intake and frequent ingestion of simple and complex carbohydrates Intramuscular injection of hydrocortisone, 50–100 mg/m^2, if oral intake not possible; activate emergency services after injection	For febrile illnesses, 2–3 times usual daily dose of glucocorticoid divided into 3 doses Increased fluid intake and frequent ingestion of simple and complex carbohydrates Intramuscular injection of hydrocortisone, 100 mg, if oral intake not possible; activate emergency services after injection
Emergency therapy¶	Hydrocortisone, 50–100 mg/m^2 (neonatal dose, 25 mg), given as IV (or intramuscular) bolus, followed by hydrocortisone, 50–100 mg/m^2 per day, divided, every 6 hr Parenteral bolus of normal (0.9%) saline, 20 ml/kg; repeated, additional fluids as clinically indicated IV bolus of dextrose, 0.5–1 g/kg, as needed for hypoglycemia	Hydrocortisone, 50–100 mg/m^2 (maximum dose, 100 mg), given as IV (or intramuscular) bolus, followed by hydrocortisone, 50–100 mg/m^2 per day, divided, every 6 hr Parenteral bolus of normal (0.9%) saline, 20 ml/kg; repeated, additional fluids as clinically indicated IV bolus of dextrose, 0.5–1 g/kg, as needed for hypoglycemia	Hydrocortisone, 100 mg, given as IV (or intramuscular) bolus, followed by hydrocortisone, 200 mg per day, divided, every 6 hr Parenteral bolus of normal (0.9%) saline, 500–1000 ml; repeated, additional fluids as clinically indicated IV bolus of dextrose, 0.5–1 g/kg, as needed for hypoglycemia
Additional considerations	Therapeutic plan for atypical genitalia should involve interdisciplinary team Increased renal sensitivity to mineralocorticoid at around 6 mo requires reduction of fludrocortisone dose Risk of hypoglycemia with illnesses	GnRH analogue may be needed for central precocious puberty‖ Children with classic CAH at risk for hypoglycemia with illnesses May need additional salt intake during hot summer months or on days of sports activities Healthy lifestyle counseling plus age-appropriate vitamin D and calcium intake recommended Patients with nonclassic CAH who are not receiving glucocorticoid therapy do not need stress dose of steroids	Patients treated for nonclassic CAH during childhood may not need therapy as adults Adolescent boys with nonclassic CAH can be weaned off treatment in midpuberty Bone mineral density and testicular adrenal rest screening during young adulthood Girls and women of reproductive age who are heterosexually active should not be treated with dexamethasone Genetic studies recommended for reproductive planning Glucocorticoid dose should be increased in third trimester for pregnant patients with classic CAH May need additional salt intake during hot summer months or on days of sports activities Healthy lifestyle counseling plus age-appropriate vitamin D and calcium intake recommended Patients with nonclassic CAH who are not receiving glucocorticoid therapy do not need stress dose of steroids

* GnRH denotes gonadotropin-releasing hormone, IV intravenous, and 17-OHP 17-hydroxyprogesterone.
† Precocious pubarche is defined as the presence of pubic hair before 8 years of age in girls and 9 years of age in boys.
‡ Measure 17-OHP, cortisol, 11-deoxycortisol, 17-hydroxypregnenolone, dehydroepiandrosterone, and androstenedione.
§ May use long-acting glucocorticoid with caution when growth is complete. To calculate daily doses, divide the hydrocortisone dose by 5 for prednisone and prednisolone, and by 80 for dexamethasone. Essential hypertension is treated with conventional agents such as calcium-channel antagonists, and fludrocortisone is continued.
¶ Fludrocortisone is not given.
‖ Central precocious puberty, due to maturation of the hypothalamic–pituitary–gonadal axis, is defined as the onset of puberty before 8 years of age in girls and 9 years of age in boys.

Adrenal disorders, management congenital adrenal hyperplasia



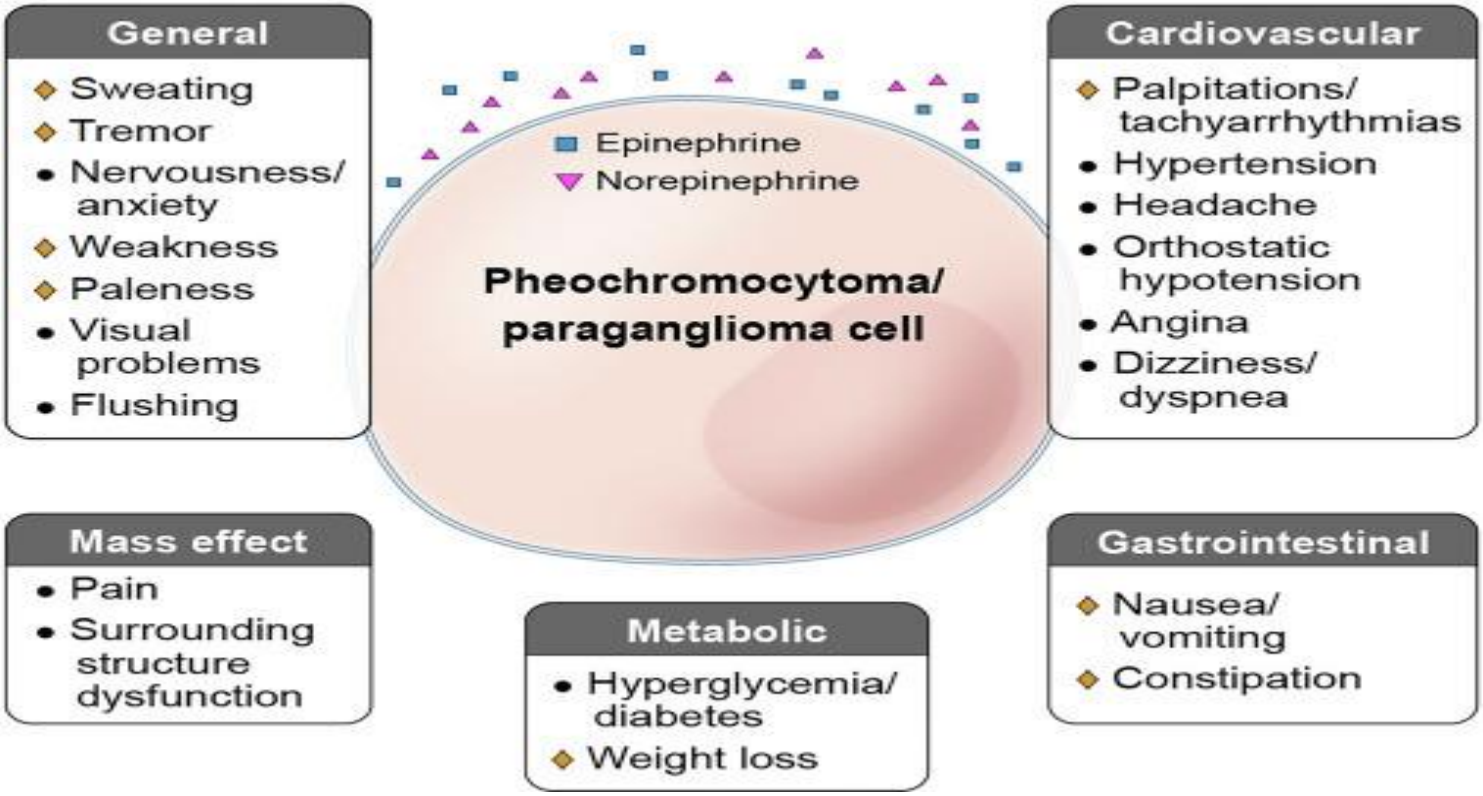
BA= bone age, SDS= standard deviations, 17-OHP= 17-hydroxyprogesterone, DHEAS= dehydroepiandrosterone sulfate, Δ5-17P 17-hydroxypregnelone, DX= Diagnosis NC-CAH=Non- Classic Congenital Adrenal hyperplasia, C-SV=Classic simple virilizing, 21-OHD=21-hydroxylase deficiency, 3βHSD= 3 beta hydroxysteroid dehydrogenase deficiency. *Criteria adapted from Lutfallah, Mermejo, and Speiser et al.

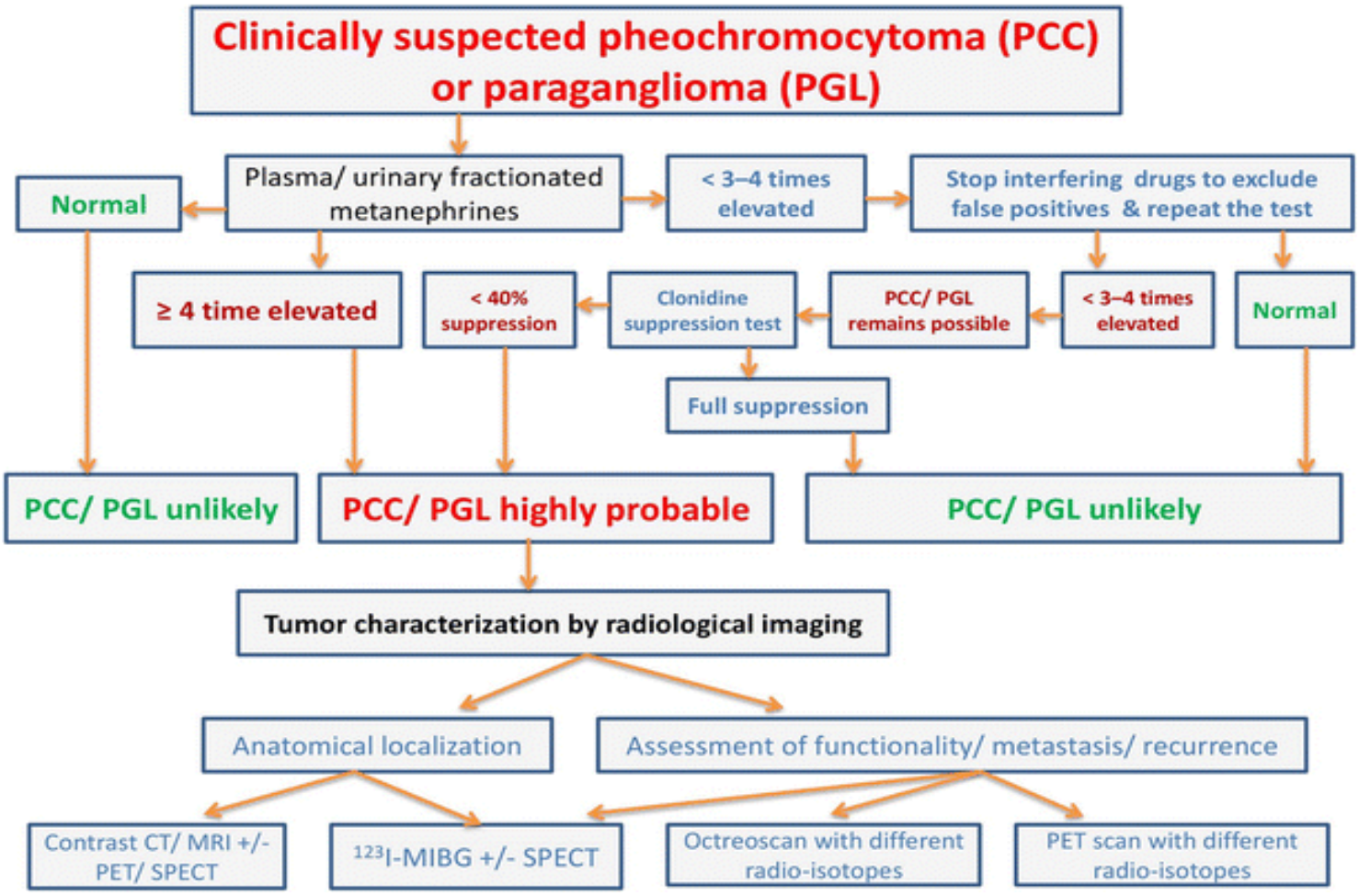


Hormonal Changes in PCOS vs Late Onset CAH

	PCOS	LO-CAH
Day 3-5 LH/FSH ratio	Sometimes elevated	Sometimes elevated (but usually less than PCOS)
Day 3-5 17-OHP	Slightly elevated	> 200 ng/dL (6 nmol/L) but can be normal
17 OHP with ACTH Stimulation	Slight elevation above normal	> 1500 ng/dL (43 nmol/L)
Prolactin	Sometimes elevated	Sometimes elevated
DHEAS	May be elevated	May be elevated
Testosterone	May be elevated	May be elevated
Androstenedione	May be elevated	May be elevated
Aldosterone	Usually Normal	Usually normal
Serum ACTH	Normal	Generally normal
Serum Cortisol	Normal or low-normal	Lower or low-normal
Ultrasound	May be polycystic phenotype	May be polycystic phenotype

Adrenal disorders, management of pheochromocytoma




Clinically suspected pheochromocytoma (PCC) or paraganglioma (PGL)
Plasma/ urinary fractionated metanephrines
Normal
< 3–4 times elevated
Stop interfering drugs to exclude false positives & repeat the test
≥ 4 time elevated
< 40% suppression
Clonidine suppression test
PCC/ PGL remains possible
< 3–4 times elevated
Normal
Full suppression
PCC/ PGL unlikely
PCC/ PGL highly probable
PCC/ PGL unlikely
Tumor characterization by radiological imaging
Anatomical localization
Assessment of functionality/ metastasis/ recurrence
Contrast CT/ MRI +/- PET/ SPECT
123I-MIBG +/- SPECT
Octreoscan with different radio-isotopes
PET scan with different radio-isotopes

False positive test, **Drugs interfering**:Acetaminophen, TCA, **Diet** : caffeine beverages & smoking

Adrenal disorders, management of pheochromocytoma

Pheochromocytoma

@Jcortesizaguirr

Epidemiology

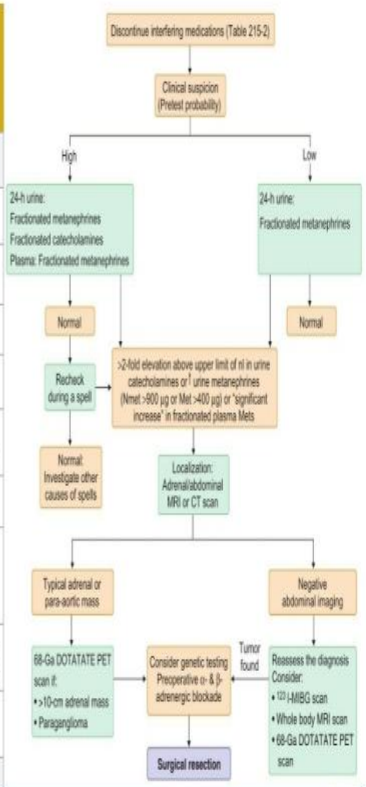
- Catecholamine-secreting neoplasms → <0.2% of pts with hypertension
- Annual incidence: 0.8/100,000 person-years
- 50-year autopsy series (1928-1977) → 50% diagnosed at autopsy
- Age range: 3rd–5th decades of life
- ♂ = ♀

10 percent rule

~10% of pheochromocytomas are extra-adrenal, multiple, bilateral, malignant, pediatric cases, not associated with hypertension, or show calcifications on imaging!

1. Spell related	2. Chronic
Anxiety/fear of impending death	Cold hands and feet
Dyspnea, diaphoresis	CHF (dilated/hypertrophic)
Epigastric/chest pain	Constipation (megacolon)
Hypertension	Diaphoresis, dyspnea
Nausea/ vomiting	Ectopic hormone secretion-dependent symptoms (CRH/ACTH, GHRH, PTH-RP, VIP)
Pallor	Epigastric/chest pain, **erythrocytosis**
Palpitation	Fatigue, fever, grade II to IV retinopathy, headache, hyperglycemia, hypertension, **livedo reticularis**
Tremor	Orthostatic hypotension, **painless hematuria (urinary bladder paraganglioma)**, palpitation
3. NOT TYPICAL of pheochromocytoma: Flushing	**Raynaud phenomenon**, tremor, weight loss

Modified from: GOLDMAN-CECIL


Discontinue interfering medications (Table 215-2)
Clinical suspicion (Pretest probability)
High
Low
24-h urine: Fractionated metanephrines Fractionated catecholamines Plasma: Fractionated metanephrines
24-h urine: Fractionated metanephrines
Normal
Normal
Recheck during a spell
>2-fold elevation above upper limit of rn in urine catecholamines or urine metanephrines (Nmet: >900 µg or Met: >400 µg) or "significant increase" in fractionated plasma Mets
Normal: Investigate other causes of spells
Localization: Adrenal/abdominal MRI or CT scan
Typical adrenal or para-aortic mass
Negative abdominal imaging
68-Ga DOTATATE PET scan if: • >10-cm adrenal mass • Paraganglioma
Consider genetic testing Preoperative α- & β-adrenergic blockade
Tumor found
Reassess the diagnosis Consider: • 123 I-MIBG scan • Whole body MRI scan • 68-Ga DOTATATE PET scan
Surgical resection

Treatment

Operable disease: Management consists of preoperative blood pressure management and then surgery.

Preoperative blood pressure management: combined alpha and beta-adrenergic blockade

First, a non-selective alpha blocker is given: phenoxybenzamine blocks alpha-1 and alpha-2 adrenoceptors equally and irreversibly.

After sufficient alpha-adrenergic blockade, a beta blocker may be started for additional blood pressure control and control of tachyarrhythmias.

Treatment of choice: laparoscopic tumor resection (adrenalectomy). **"No-touch" technique**

Open surgical resection is reserved for large or invasive tumors.

Starting beta blockers before alpha blockade is contraindicated. ***Beta blockers*** cancel out the vasodilatory effect of peripheral beta-2 adrenoceptors, potentially leading to unopposed alpha-adrenoceptor stimulation, causing vasoconstriction and ultimately hypertensive crisis. **Inoperable disease**

Benign pheochromocytoma: primary therapy with phenoxybenzamine

Malignant pheochromocytoma: MIBG therapy; otherwise, palliative treatment (chemotherapy, tumor embolization)

Etiology

1. Arise from chromaffin cells → neural crest
2. Localization:
   - **~90% adrenal medulla** (physiologically activated by acetylcholine)
   - **~10% extra-adrenal** in the sympathetic ganglia
   - **~10% at multiple locations**
- **40%** → familial disorders:
  - Multiple endocrine neoplasia type 2 **(MEN 2A, MEN 2B) (50% of pts** w/ MEN2 have pheochromocytoma)
  - **Neurofibromatosis type 1 (NF1)** (0.1-5.7%)
  - **Von Hippel-Lindau (VHL) disease** (10-20%)

Clinical features

1. History in a symptomatic patient, discovery of an incidental adrenal mass, or the family history in a patient with familial disease.

Symptoms and signs: 50% pts, and when present, they are typically paroxysmal.

Classic triad: episodic headache, sweating, and tachycardia (don't trust triads)

Hypertension: ½ paroxysmal HTN, most primary hypertension; **some normal BP** (5-15%) → incidentaloma/periodic screening for familial pheochromocytoma.

Headache → mild or severe → 90% of symptomatic patients

Generalized sweating → 60-70% symptomatic; forceful palpitations, tremor, pallor, dyspnea, generalized weakness, and panic attack-type symptoms.

Pheochromocytoma crisis, or pheochromocytoma multisystem crisis → These individuals may have either **hypertension or hypotension**, hyperthermia (temperature >40°C), mental status changes, and other organ dysfunction.

Less common symptoms and signs:

Orthostatic hypotension (may reflect low plasma volume) **and others** → visual blurring, papilledema, weight loss, polyuria, polydipsia, constipation, increased erythrocyte sedimentation rate, **insulin resistance, hyperglycemia, leukocytosis**, psychiatric disorders, and, rarely, **secondary erythrocytosis** due to overproduction of erythropoietin

Cardiomyopathy → cardiomyopathy attributed to catecholamine excess that is similar to stress-induced (takotsubo) cardiomyopathy; may present with → pulmonary edema (deteriorate w/ initiation of beta-adrenergic blockade

Paroxysmal elevations in blood pressure → pheochromocytoma when → paroxysmal elevations in blood pressure (hypertension, tachycardia, or arrhythmia) during **diagnostic procedures (eg, colonoscopy), induction of anesthesia, surgery, with certain foods or beverages containing tyramine, or with certain drugs** (such as beta-adrenergic blockers, tricyclic antidepressants, corticosteroids, metoclopramide or monoamine oxidase inhibitors [MAOIs])

Abnormalities in carbohydrate metabolism → (insulin resistance, impaired fasting glucose, apparent type 2 diabetes mellitus) are directly related to the **increase in catecholamine production. Diabetes** is present in **one in three** patients with pheochromocytoma. In young patients with hypertension and normal body weight, the presence of diabetes is a clinical clue to the diagnosis of pheochromocytoma.

10 percent rule = 10% of pheochromocytomas are extra-adrenal, multiple, bilateral, malignant, pediatric cases, not associated with hypertension, or calcifications showing on imaging

Adrenal disorders, management of Hyperhydrosis

Box 1: Causes of generalized[12] and focal hyperhidrosis[13]

Focal hyperhidrosis

Primary idiopathic hyperhidrosis
Gustatory sweating (Frey's syndrome)
Neurologic
- Neuropathies
- Spinal injury

Generalized hyperhidrosis

Endocrine
- Hyperthyroidism
- Hyperpituitarism
- Diabetes mellitus
- Menopause
- Pregnancy
- Pheochromocytoma
- Carcinoid syndrome
- Acromegaly

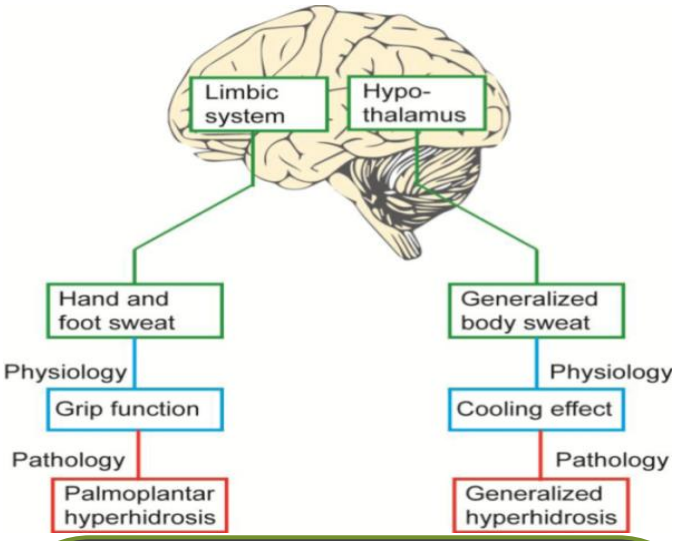
Neurologic
- Parkinson's disease
- Spinal cord injury
- Cerebrovascular accident

Malignant disease
- Myeloproliferative disorders
- Hodgkin's disease

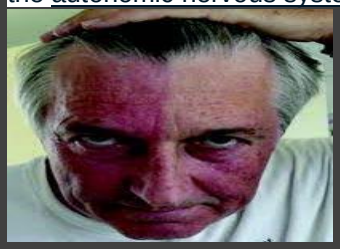
Infection
Cardiovascular
- Shock
- Heart failure

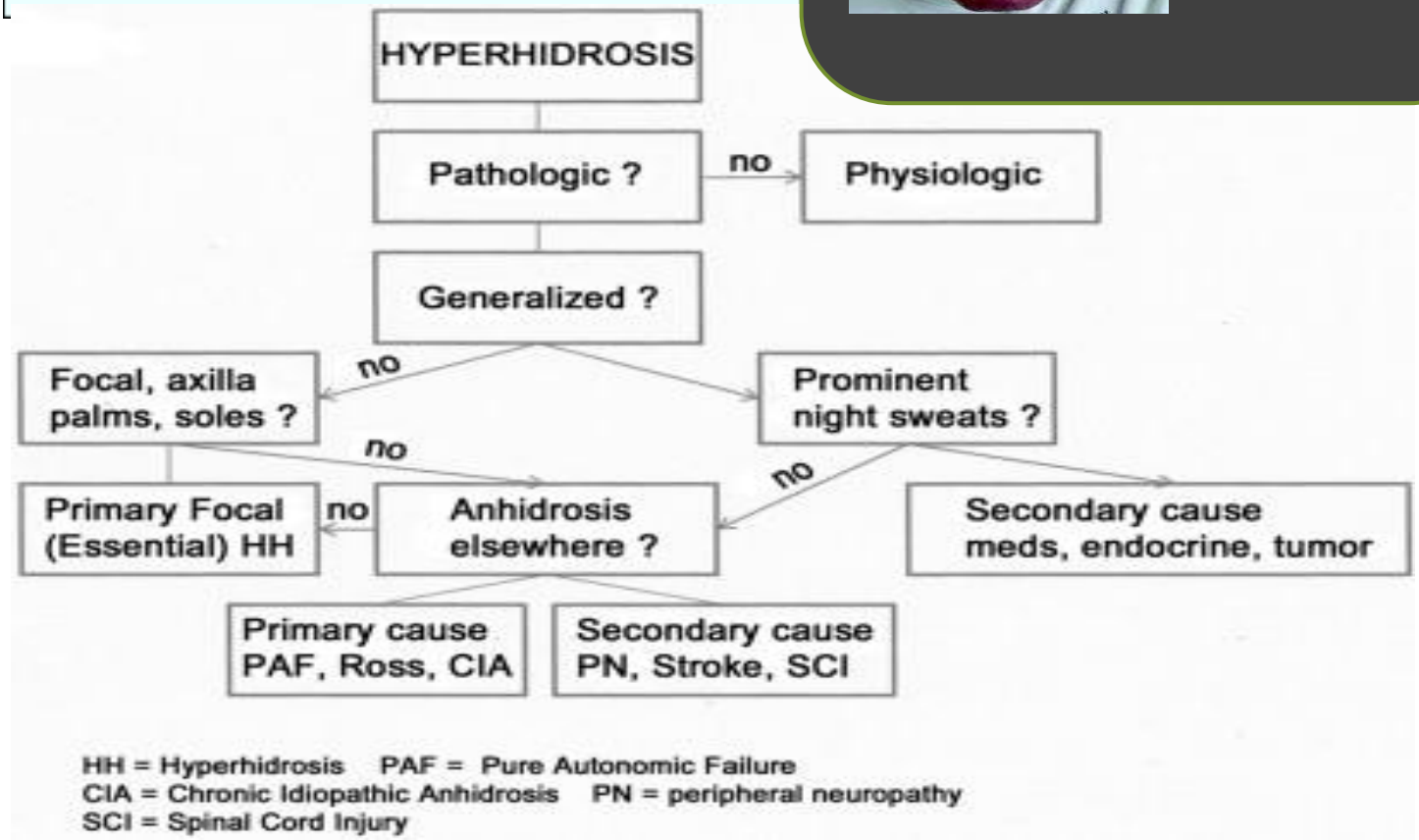
Respiratory failure
Drugs
- Fluoxetine
- Venlafaxine
- Doxepin

Toxicity
- Alcoholism
- Substance abuse



Harlequin syndrome is a condition characterized by asymmetric sweating and flushing on the upper thoracic region of the chest, neck and face. Harlequin syndrome is considered an injury to the autonomic nervous system (ANS).



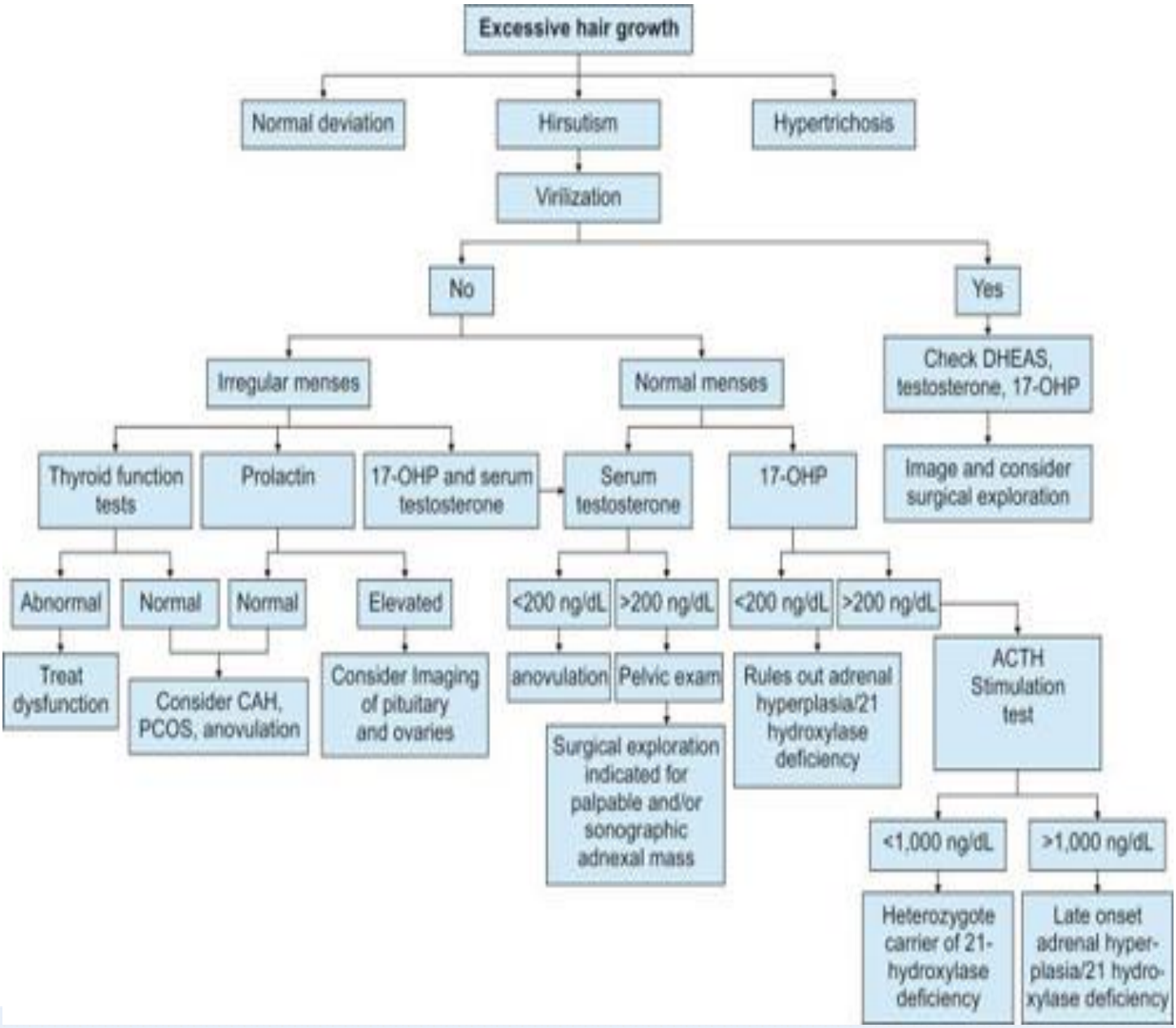


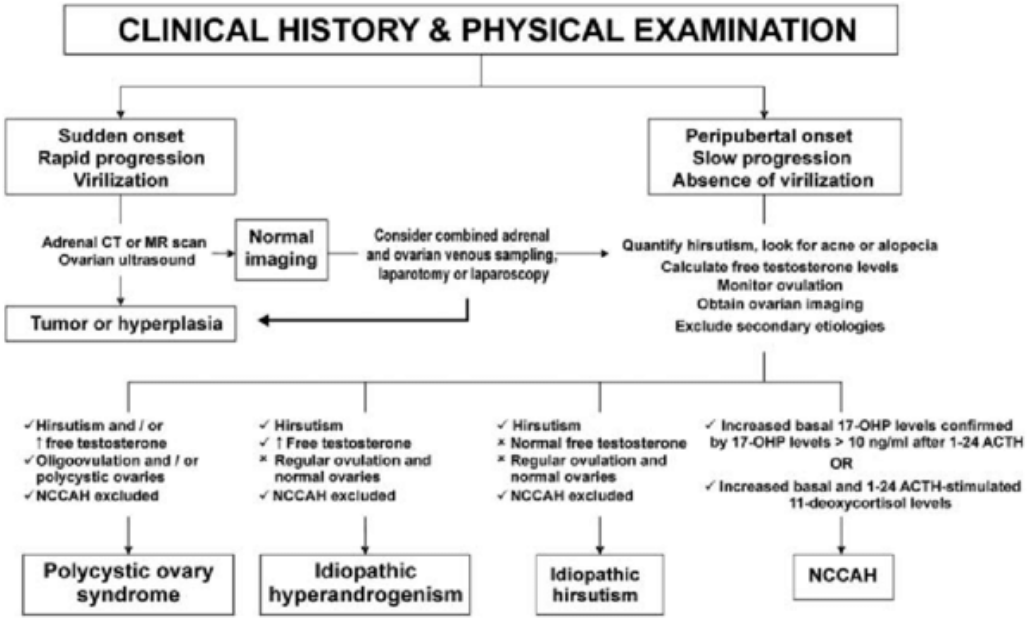
Adrenal disorders, management of pheochromocytoma

Remember Hyperhydrosis could be generalized or focal

Type of Treatment	OTC Antiperspirant (Metallic Salts: Aluminum Chloride, Zirconium)	Clinical Strength Antiperspirant (Aluminum Chloride Hexahydrate: Certain Dri® and Drysol)	Iontophoresis	Botox® (OnabotulinumtoxinA)	miraDry®	Local Excision of Axillary Sweat Glands (Tumescent Liposuction)	Endoscopic Thoracic Sympathectomy (ETS)	Oral Medication (Anticholinergics)
How the Treatment Is Performed	Applied topically to reduce sweat and odor	Applied topically to reduce sweat and odor	Electricity is applied to the extremities through a tray of water in which the hand or foot sits.	Botox® is injected into the affected area in a grid pattern.	Electromagnetic energy applied to underarms	Minimally invasive surgery of the underarms	Minimally invasive endoscopic procedure	Taken orally
How It Works	Antiperspirants plug ducts that are located on the surface of the skin.	Antiperspirants plug ducts that are located on the surface of the skin.	A gentle electrical current temporarily disables the sweat gland.	Interrupts the nerve signal that stimulates the sweat gland	Electromagnetic energy eliminates the glands that cause sweat and odor.	The sweat glands located in subcutaneous fat are removed via liposuction.	The sympathetic nerve chain in the thoracic cavity is interrupted to reduce the nerve signaling that stimulates sweat glands.	Blocks nerve transmissions that trigger the sweat glands
Duration of Effect	~ 24 hours or less	~ 24 hours or less	1 day to 1 week, depending on the individual	~ 3-6 months	Permanent	Permanent	Permanent	~ 24 hours
Number of Treatments Required	As needed daily	As needed daily	3x a week initially, then 1x per week once results are achieved	2-4x/year	1-2 treatments	1 treatment	1 treatment	Daily
Advantage(s)	• Noninvasive • Can be used in more than one location	• Noninvasive • Can be used in more than one location • Stronger than OTC antiperspirant	• Can be successful for patients with palmar and plantar (foot) hyperhidrosis • No recovery time • Can be done at home	• Fast • Minimally invasive • Can be used in multiple locations • No recovery time • Widely available	• FDA-approved to eliminate sweat or odor • Reduces hair from underarms • Minimally invasive • Minimal to no recovery time	• Minimally invasive • Minimal recovery time	• Minimally invasive • High success rates • Minimal recovery time • Results are immediate	**For patients who:** • Can treat generalized sweat and multi-focal hyperhidrosis
Disadvantages and Possible Side Effects	• Results are temporary • Must be reapplied as needed • Contains chemical toxins • Skin irritation that can lead to infection	• Results are temporary • Must be reapplied as needed • Contains high amounts of aluminum chloride • Skin irritation that can lead to infection	• Often must be performed on a daily basis to maintain results • Time consuming daily treatment **Can cause:** • Dryness • Blistering • Peeling • Irritation	• Must be repeated 2-4x /year to maintain results • Patients can build a tolerance to the treatment, rendering it less effective • Does not treat odor **Can cause:** • Headache • Muscle stiffness • Neck/back pain • Drowsiness **At or near injection site:** • Muscle weakness • Bruising • Pain • Swelling	• Currently not covered by health insurance **Can cause:** • Mild, temporary swelling • Bruising • Temporary numbness	• Repeat surgery may be necessary to achieve results • Post-procedure recovery time is needed • Results can vary and be inconsistent	• Post procedure recovery time is needed • Possibility of compensatory sweating	**Can cause:** • Dry mouth • Constipation • Difficulty voiding • Palpitation
Area Treated (Bold= Most effective)	• **Underarms** • Hands • Feet	• **Underarms** • Hands • Feet	• **Hands** • **Feet**	• Hands • **Scalp** • Face • **Underarms** • Feet	• **Underarms**	• **Underarms**	• **Hands** • **Feet** • **Underarms**	• **Head** • **Face** • **Generalized**

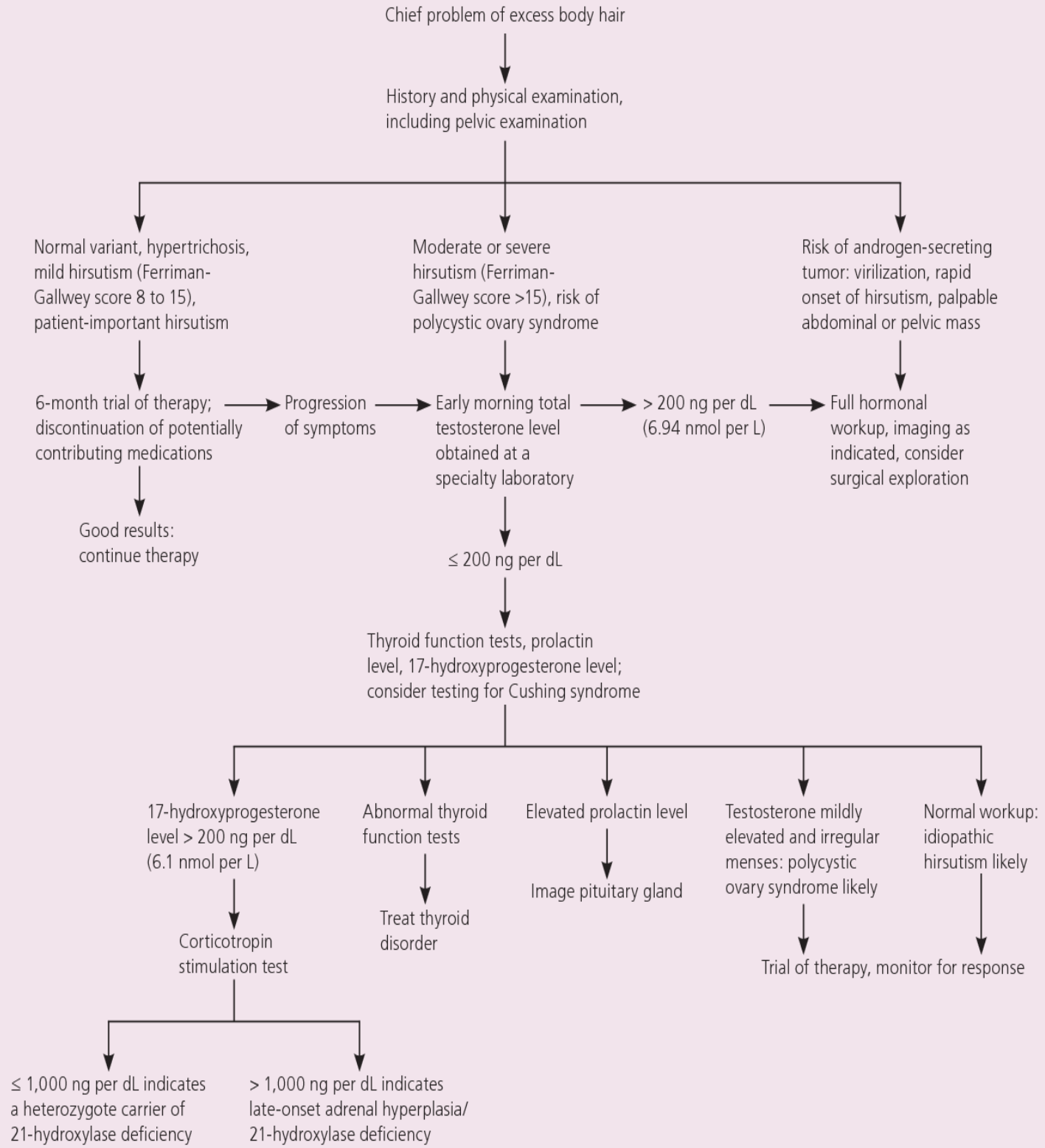
Adrenal disorders, management of Hirsutism *





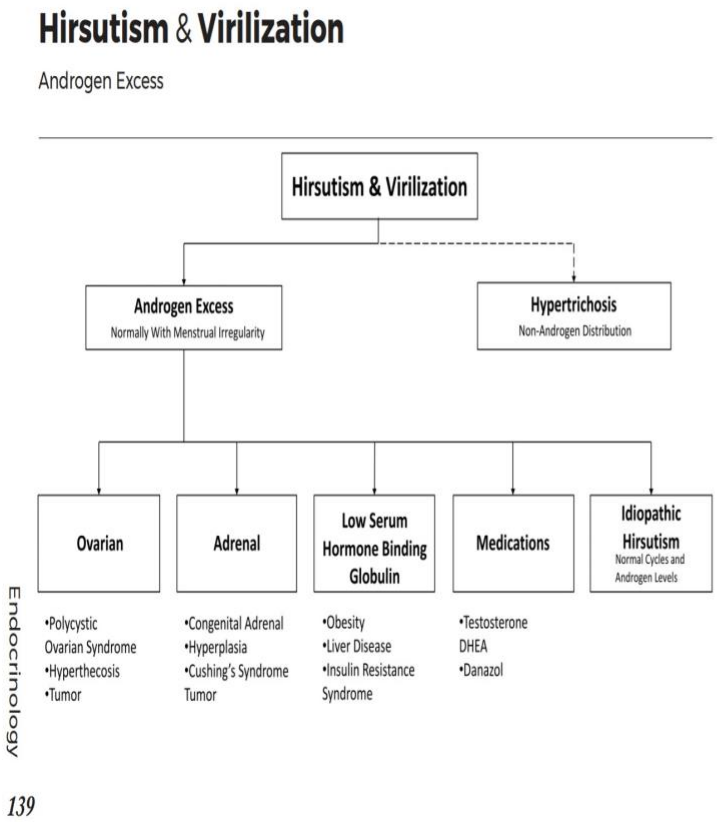
Adrenal disorders, management of Hirsutism

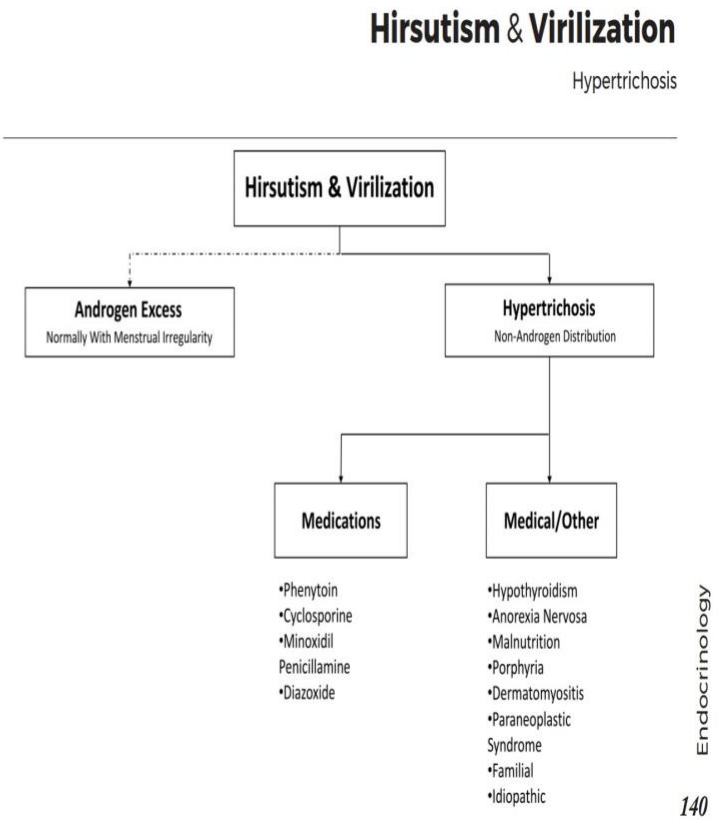
Evaluation of Hirsutism in Women


Chief problem of excess body hair
History and physical examination, including pelvic examination
Normal variant, hypertrichosis, mild hirsutism (Ferriman-Gallwey score 8 to 15), patient-important hirsutism
Moderate or severe hirsutism (Ferriman-Gallwey score >15), risk of polycystic ovary syndrome
Risk of androgen-secreting tumor: virilization, rapid onset of hirsutism, palpable abdominal or pelvic mass
6-month trial of therapy; discontinuation of potentially contributing medications
Progression of symptoms
Early morning total testosterone level obtained at a specialty laboratory
> 200 ng per dL (6.94 nmol per L)
Full hormonal workup, imaging as indicated, consider surgical exploration
Good results: continue therapy
≤ 200 ng per dL
Thyroid function tests, prolactin level, 17-hydroxyprogesterone level; consider testing for Cushing syndrome
17-hydroxyprogesterone level > 200 ng per dL (6.1 nmol per L)
Abnormal thyroid function tests
Elevated prolactin level
Testosterone mildly elevated and irregular menses: polycystic ovary syndrome likely
Normal workup: idiopathic hirsutism likely
Corticotropin stimulation test
Treat thyroid disorder
Image pituitary gland
Trial of therapy, monitor for response
≤ 1,000 ng per dL indicates a heterozygote carrier of 21-hydroxylase deficiency
> 1,000 ng per dL indicates late-onset adrenal hyperplasia/ 21-hydroxylase deficiency

Remember , DON't forget Late onset Congenital adrenal hyperplasia

Adrenal disorders, management of Hirsutism & virilization





VIRILZATION IN A FEMALE

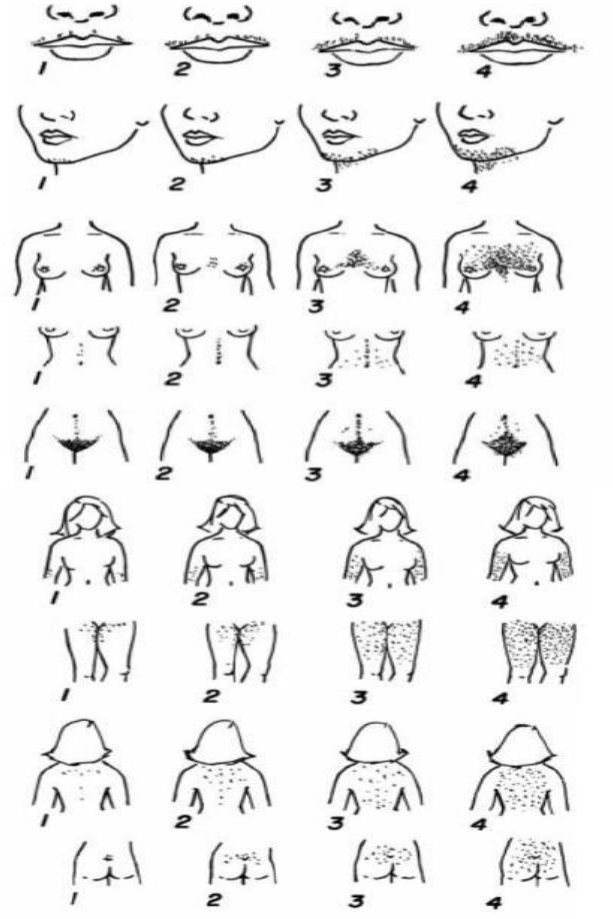
- male pattern baldness
- excessive facial hair, usually on your cheeks, chin, and upper lip
- deepening of your voice
- small breasts
- enlarged clitoris
- irregular menstrual cycles
- increased sex drive

Ferriman-Gallwey score of 8 or more was considered diagnostic of hirsutism

Ferriman Gallway Score

Naam: _____
Geboortedatum: ____ / ____ / _____
Patientnummmer: _____

SCORE: _____ (>8: hirsutisme)



Bovenlip
- Geen haar 0
- Een paar haren boven de mondhoeken 1
- Een kleine snor (niet tot aan de middellijn) 2
- Een kleine snor tot aan de middellijn 3
- Een snor over de gehele bovenlip 4

Kin
- Geen haar 0
- Een paar donkere haren 1
- Donkere haren in kleine concentraties 2
- Geheel bedekt (licht) 3
- Geheel bedekt (zwaar) 4

Borst
- Geen haar 0
- Haar rond de tepel 1
- Haar rond tepel en op borstbeen 2
- Driekwart bedekt met haar 3
- Helemaal bedekt 4

Bovenbuik
- Geen haar 0
- Paar haren op de middellijn 1
- Meerdere haren op de middellijn 2
- Half bedekt 3
- Geheel bedekt 4

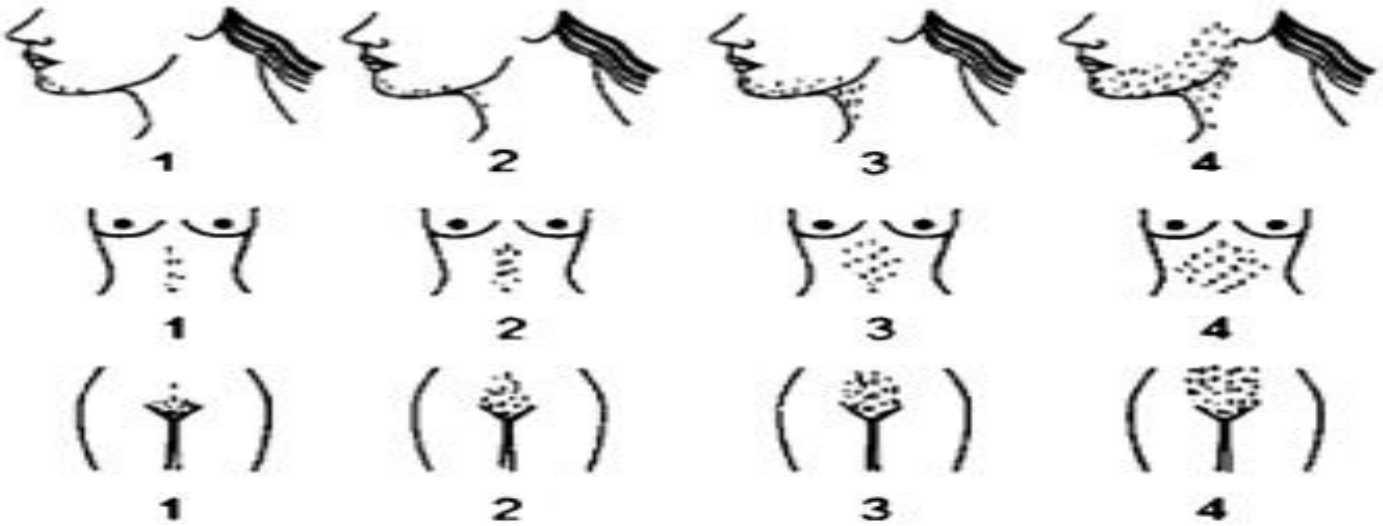
Onderbuik (onder navel)
- Geen haar 0
- Haar op de middellijn 1
- Streep haar op de middellijn 2
- Band haar op de middellijn 3
- V-vormige groei 4

Bovenarm
- Geen haar 0
- Een paar donkere haren 1
- Meerdere donkere haren 2
- Geheel bedekt (licht) 3
- Geheel bedekt (zwaar) 4

Dijbeen
- Geen haar 0
- Weinig / minder dan een kwart bedekt 1
- Meer, maar niet volledig bedekt 2
- Geheel bedekt (licht) 3
- Geheel bedekt (zwaar) 4

Bovenrug
- Geen haar 0
- Een paar donkere haren 1
- Meerdere donkere haren 2
- Geheel bedekt (licht) 3
- Geheel bedekt (zwaar) 4

Onderrug
- Geen haar 0
- Pluk haar onderaan rug 2
- Geheel bedekt 4

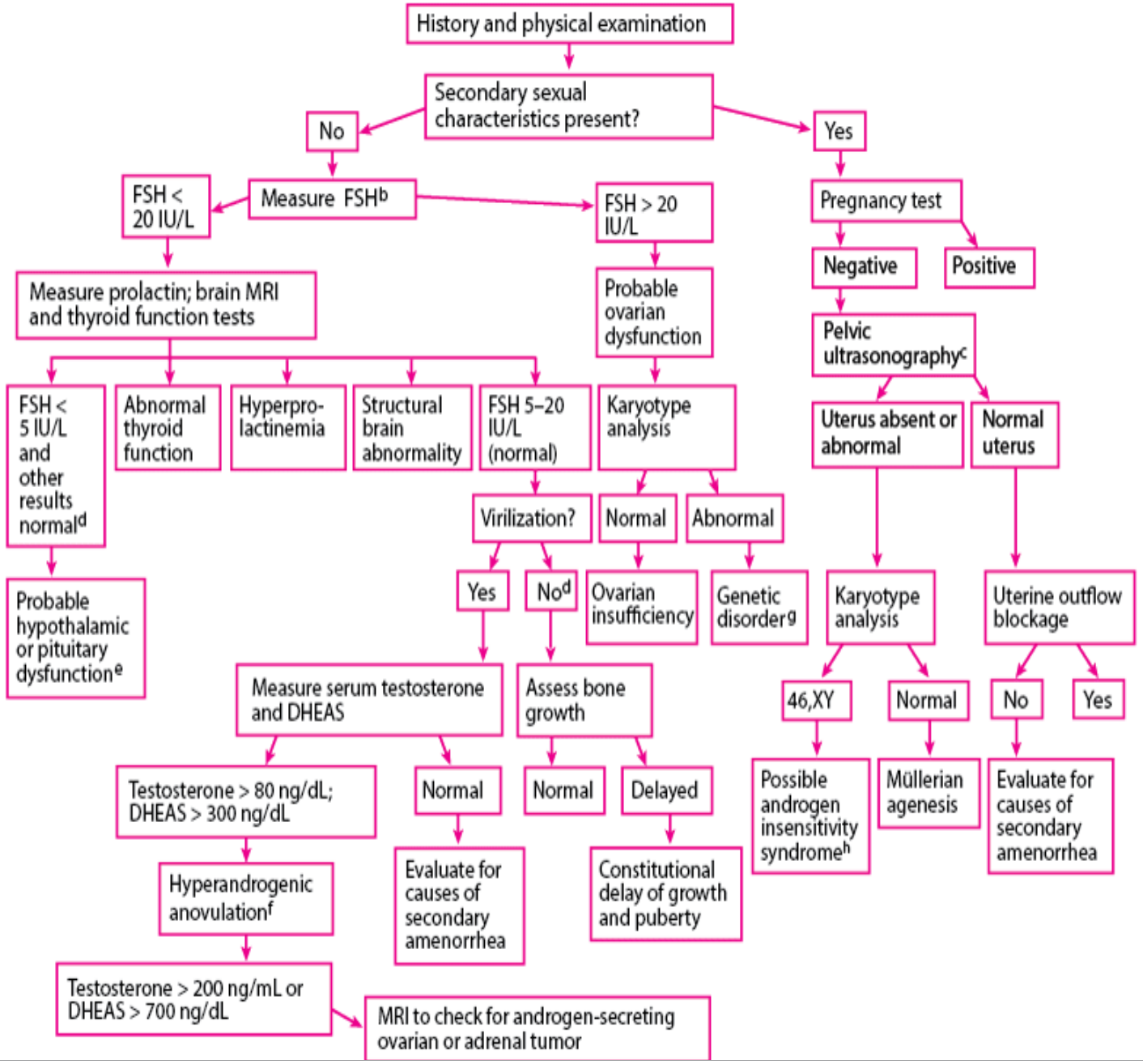


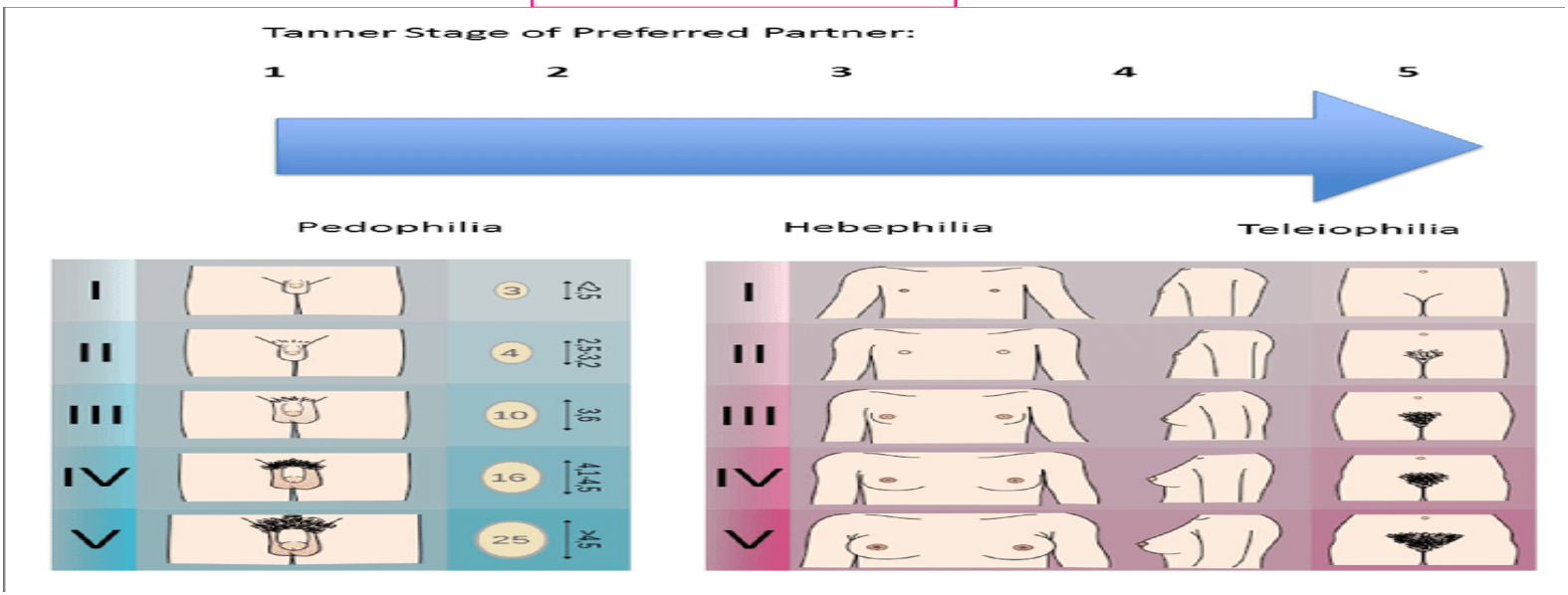
Circle affected area

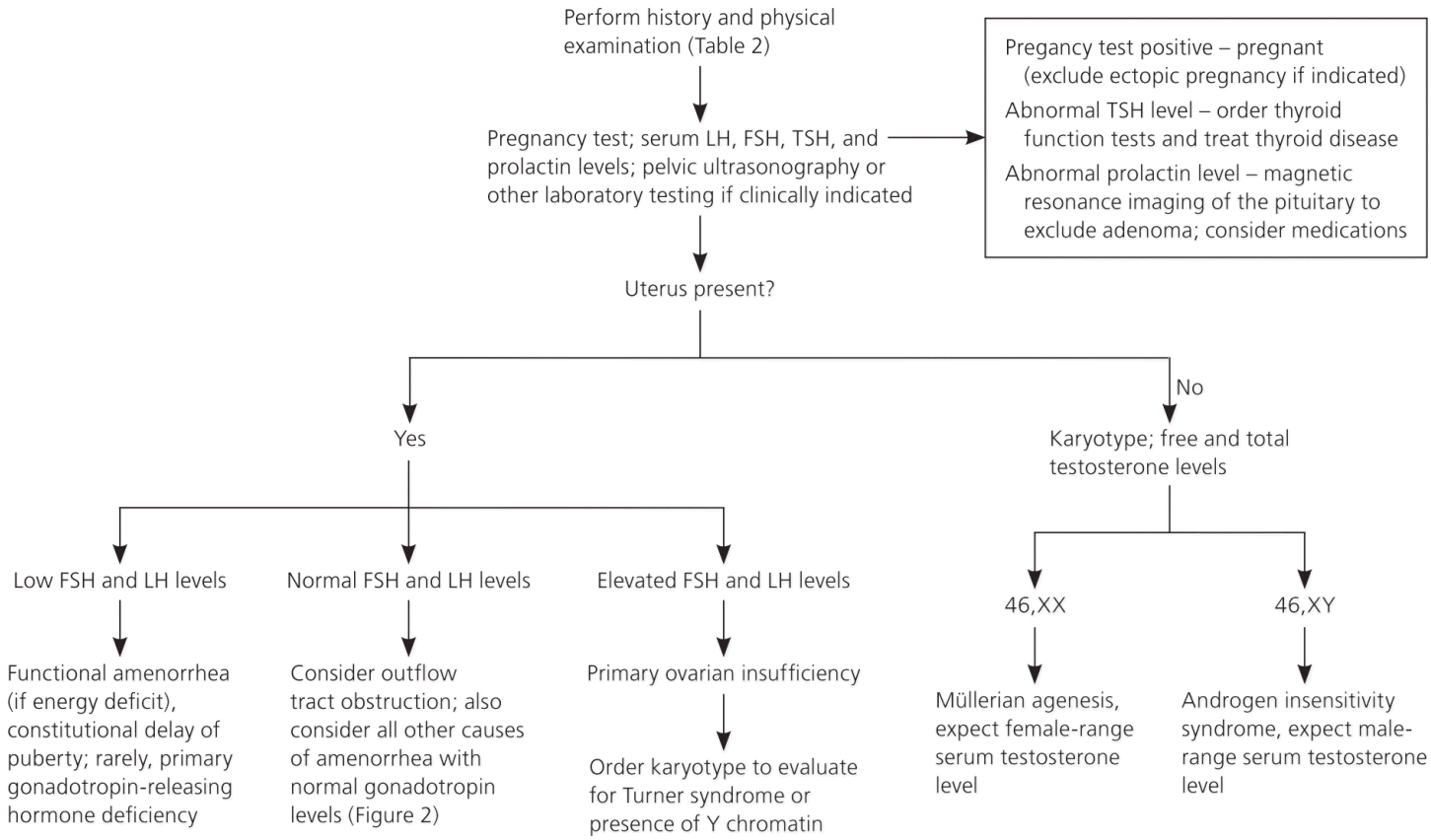
Total simplified Ferriman-Gallwey (sFG) score: _____

An sFG score of ≥3 is highly predictive of hirsutism

Gonadal Disorders management of primary Amenorrhea



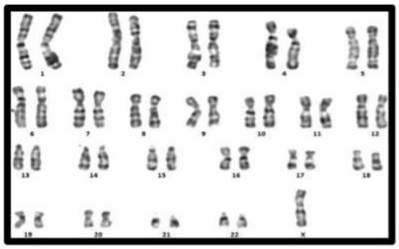



Perform history and physical examination (Table 2)
Pregnancy test; serum LH, FSH, TSH, and prolactin levels; pelvic ultrasonography or other laboratory testing if clinically indicated
Pregancy test positive – pregnant (exclude ectopic pregnancy if indicated)
Abnormal TSH level – order thyroid function tests and treat thyroid disease
Abnormal prolactin level – magnetic resonance imaging of the pituitary to exclude adenoma; consider medications
Uterus present?
Yes
No
Low FSH and LH levels
Normal FSH and LH levels
Elevated FSH and LH levels
Karyotype; free and total testosterone levels
Functional amenorrhea (if energy deficit), constitutional delay of puberty; rarely, primary gonadotropin-releasing hormone deficiency
Consider outflow tract obstruction; also consider all other causes of amenorrhea with normal gonadotropin levels (Figure 2)
Primary ovarian insufficiency
Order karyotype to evaluate for Turner syndrome or presence of Y chromatin
46,XX
46,XY
Müllerian agenesis, expect female-range serum testosterone level
Androgen insensitivity syndrome, expect male-range serum testosterone level

Breasts Present/Uterus Absent	Müllerian Agenesis (46,XX)	Androgen Insensitivity (46,XY)
Uterus absent?	Idiopathic	MIF
Estrogen from?	Ovaries	Testes
Pubic hair?	Present	Absent
Testosterone level?	Female	Male
Treatment	No hormones Create vagina IVF—surrogate	Estrogen Create vagina Remove testes

Characteristic findings	MRKH/ MURCS	Isolated vaginal atresia	WNT4 syndrome	Androgen insensitivity
Upper vagina	Absent	Variable	Absent	Absent
Uterus	Absent	Present	Absent	Absent
Gonads	Ovary	Ovary	Masculinized ovary	Testis
Breast development	Normal	Normal	Normal	Normal
Pubic-hair development	Normal	Normal	Normal	Sparse
Hyperandrogenism	No	No	Yes	No
Karyotype	46, XX	46, XX	46, XX	46, XY

MRKH: Mayer–Rokitansky–Kuster–Hauser, MURCS: Müllerian duct aplasia, Renal dysplasia and Cervical Somite anomalies, AIS: Androgen insensitivity syndrome



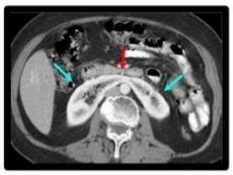
4) Turner Syndrome

❖ **Clinical features**
- ✓ Short stature
- ✓ Lymphedema of hands & feet
- ✓ Shield chest
- ✓ Cubitus valgus
- ✓ Low posterior hairline
- ✓ Posterior rotated ears
- ✓ Webbed neck
- ✓ Short 4th metacarpal bone
- ✓ Normal intelligence (except Math)

❖ **What is the most consistent finding?**
- ✓ Short stature (SHOX gene)
- ✓ Ovarian dysgenesis

❖ **What is the most common cardiac defect?**
1. Bicuspid aortic valve
2. Coarctation of aorta

❖ **Labs finding ?**
- ✓ High FSH
- ✓ High FSH/LH
- ✓ Low estradiol



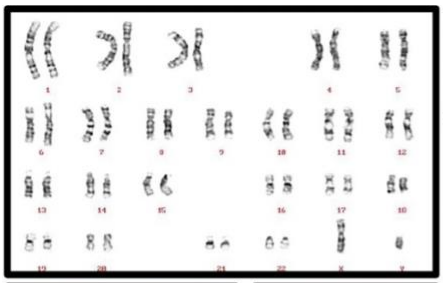
❖ **What is the most common renal anomaly ?**
- ✓ Horseshoe kidney
- ✓ Double collecting system

❖ **Increases risk of :**
- ✓ Hypothyroidism
- ✓ Hashimoto disease
- ✓ Celiac disease
- ✓ Inflammatory bowel disease

Pediatric On Squores

❖ **Increases risk of which Malignancy ?**
- ✓ Gonadoblastoma

❖ **Treatment**
- ✓ Growth hormone
- ✓ Estrogen therapy



5) Noonan Syndrome

❖ **Clinical features**
- ✓ **Down slanting palpebral fissures**
- ✓ Short stature
- ✓ Shield chest
- ✓ Cubitus valgus
- ✓ Low posterior hairline
- ✓ Webbed neck
- ✓ Posterior rotated ears
- ✓ Cryptorchidism
- ✓ Intellectual disability
- ✓ Delayed puberty
- ✓ Ptosis

Pediatric On Squores

❖ **Mode of inheritance?**
- ✓ Autosomal dominant
- ✓ PTPN11 gene on 12q24
- ✓ Normal karyotype

❖ **What is the most common cardiac defect?**
1. Pulmonary stenosis
2. Hypertrophic cardiomyopathy

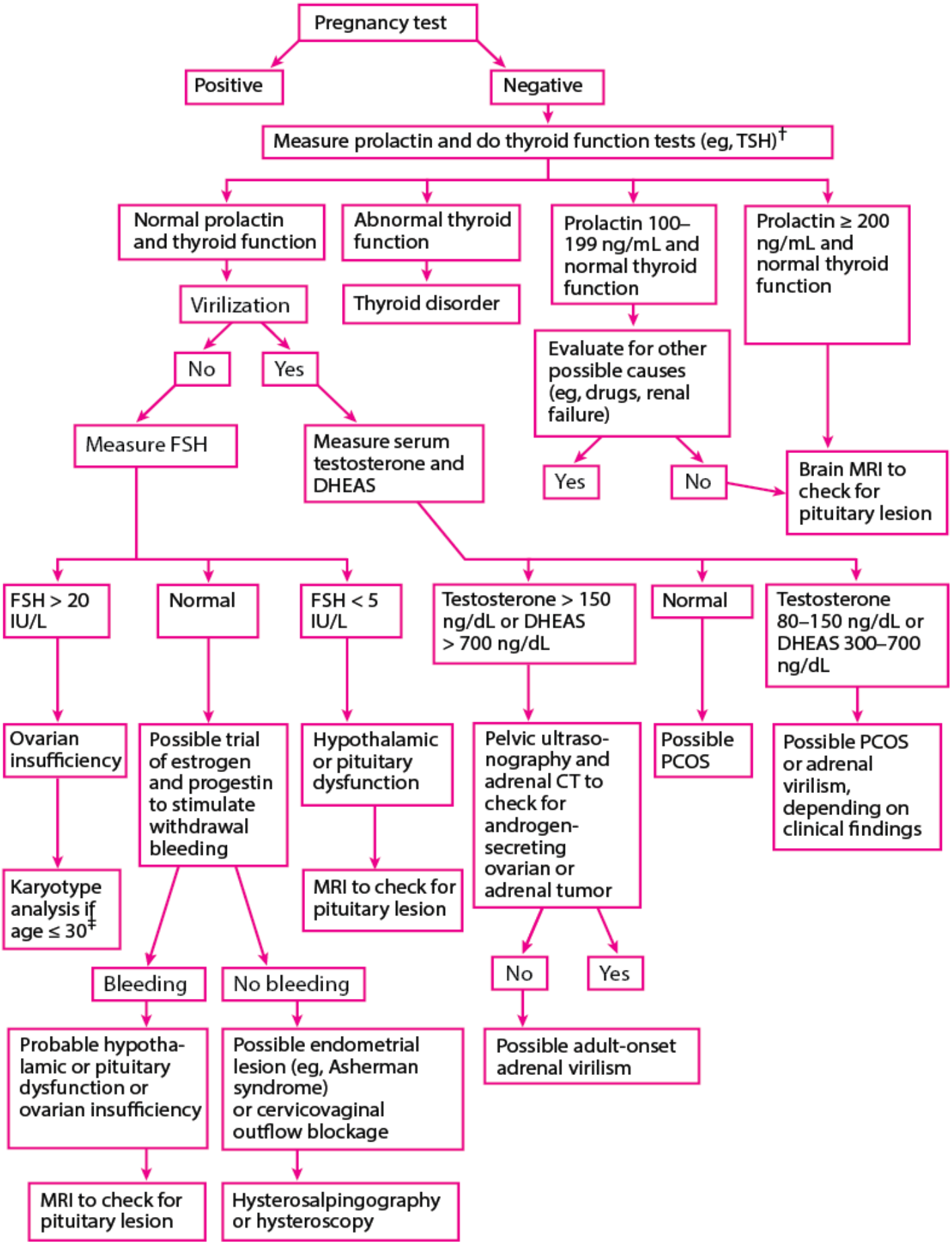
❖ **Labs finding ?**
- ✓ Clotting factor deficiencies
  - Mainly factor XI & XII
- ✓ Abnormal platelet count/function

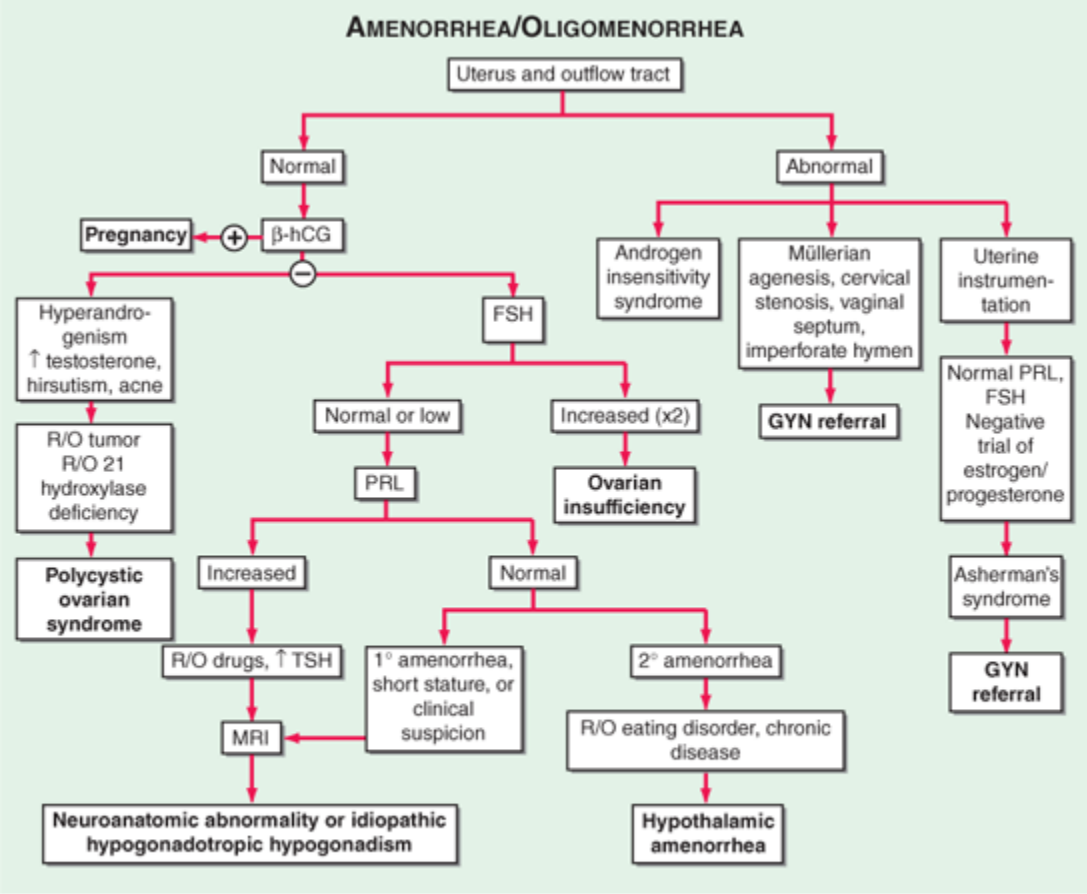
❖ **Increases risk of which Malignancy ?**
- ✓ Acute lymphocytic leukemia (ALL)
- ✓ Chronic myeloid leukemia (CML)

❖ **Treatment**
- ✓ Growth hormone

@OnSquares

Gonadal Disorders management of secondary Amenorrhea


Pregnancy test
Positive
Negative
Measure prolactin and do thyroid function tests (eg, TSH)†
Normal prolactin and thyroid function
Abnormal thyroid function
Prolactin 100–199 ng/mL and normal thyroid function
Prolactin ≥ 200 ng/mL and normal thyroid function
Virilization
Thyroid disorder
Evaluate for other possible causes (eg, drugs, renal failure)
No
Yes
Measure FSH
Measure serum testosterone and DHEAS
Yes
No
Brain MRI to check for pituitary lesion
FSH > 20 IU/L
Normal
FSH < 5 IU/L
Testosterone > 150 ng/dL or DHEAS > 700 ng/dL
Normal
Testosterone 80–150 ng/dL or DHEAS 300–700 ng/dL
Ovarian insufficiency
Possible trial of estrogen and progestin to stimulate withdrawal bleeding
Hypothalamic or pituitary dysfunction
Pelvic ultrasonography and adrenal CT to check for androgen-secreting ovarian or adrenal tumor
Possible PCOS
Possible PCOS or adrenal virilism, depending on clinical findings
Karyotype analysis if age ≤ 30‡
MRI to check for pituitary lesion
Bleeding
No bleeding
No
Yes
Probable hypothalamic or pituitary dysfunction or ovarian insufficiency
Possible endometrial lesion (eg, Asherman syndrome) or cervicovaginal outflow blockage
Possible adult-onset adrenal virilism
MRI to check for pituitary lesion
Hysterosalpingography or hysteroscopy



Source: J.L Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Manual of Medicine, Twentieth Edition.
Copyright © McGraw-Hill Education. All rights reserved.

1. Administer oral medroxyprogesterone acetate for 5–10 days.

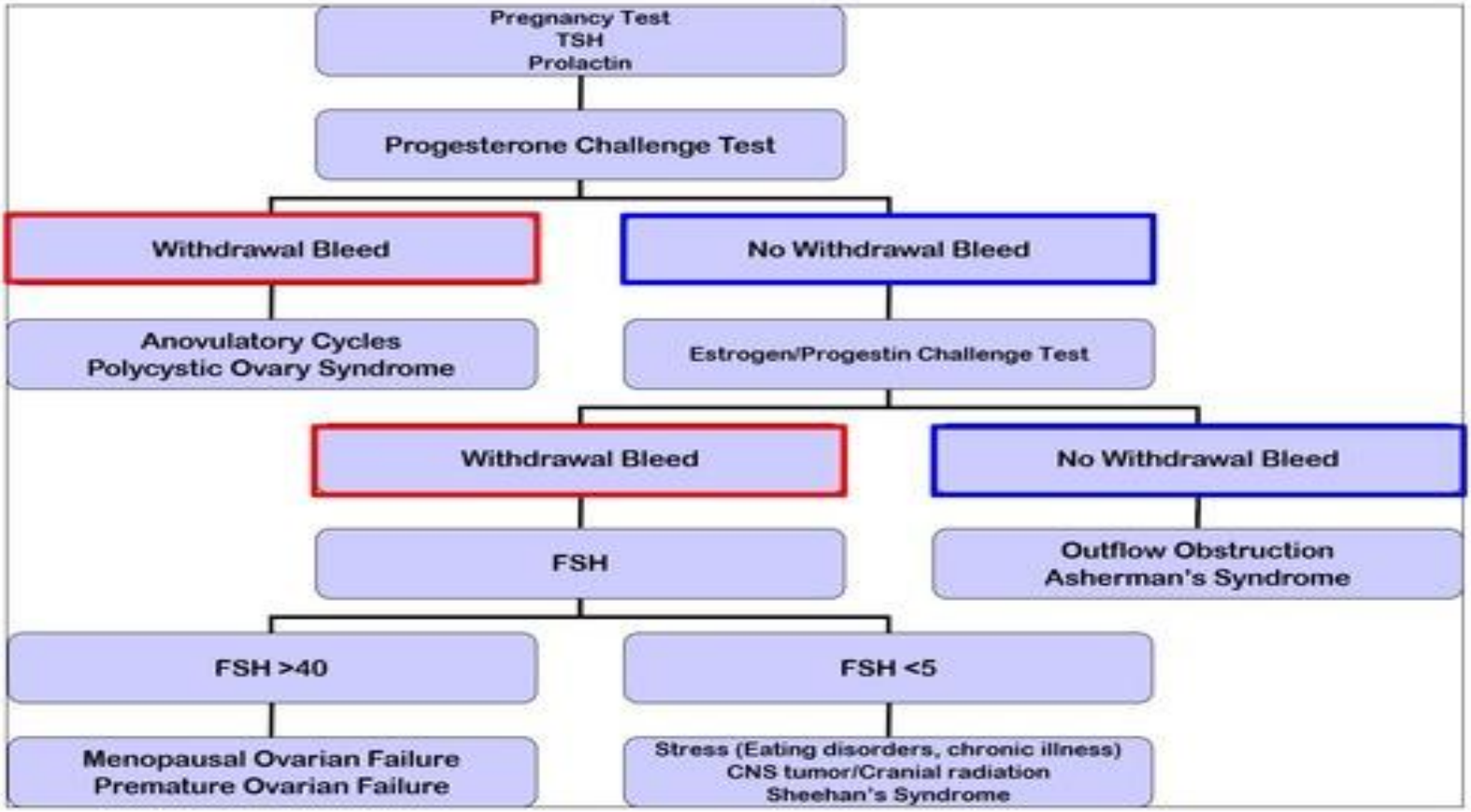
2. Look for withdrawal bleeding after medroxyprogesterone cessation.

A positive response:

- Any bleeding more than light spotting that occurs within 2 weeks after the progestin is given
- Will usually occur 2–7 days after the progestin is finished

Gonadal Disorders management of secondary Amenorrhea

Evaluation of Secondary Amenorrhea: Progesterone Challenge Test



POI patients recruited for assessment from the Reproductive Center Affiliated to Shandong University (collected during February 2006–April 2018)

↓

Serum test
FSH, E2, AMH (if available)

Pelvic ultrasonography
Ovary size, antral follicle counts

Medical history
Past history, family history, pregnancy history, menstrual history

Exclusion criteria

✓ Chromosomal abnormalities

✓ Iatrogenic factors
- Radiation therapy
- Chemotherapy
- Ovarian surgery (including unilateral and bilateral ovarian surgery for endometrioma)

✓ Autoimmune factors
- Addison's disease
- Autoimmune thyroid disease
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Antinuclear antibodies positivity

Add criteria*
- Age <40
- FSH >25 IU/L (two occasions >4 weeks apart)
- Oligomenorrhea or amenorrhea (>4 months)

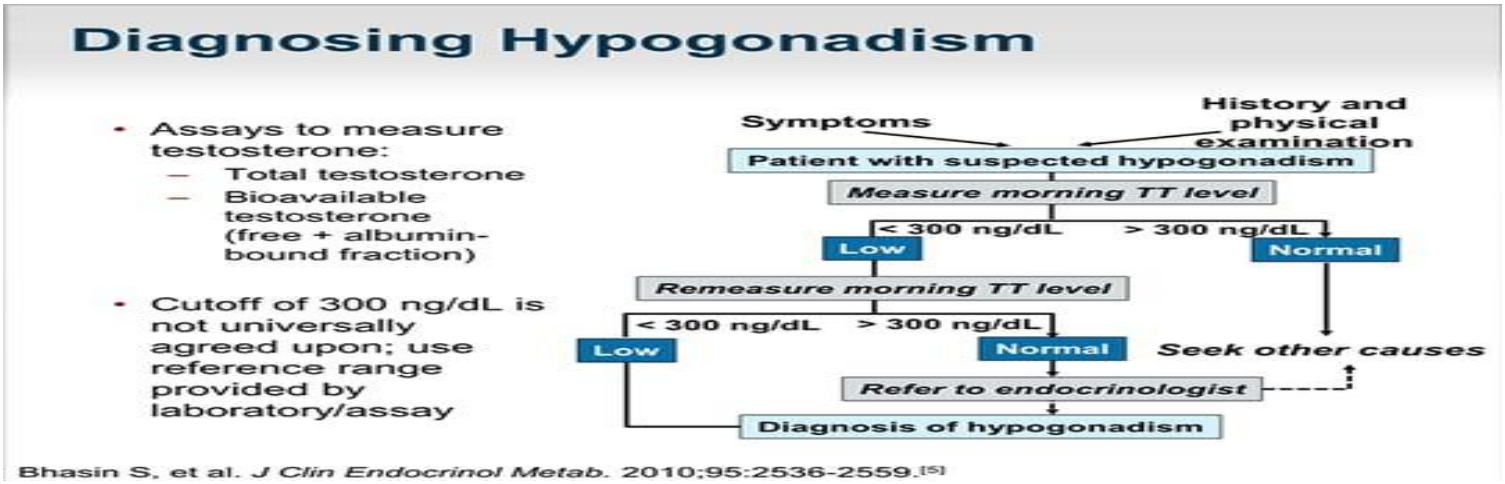
↓

Cohort of patients with idiopathic POI, possibly attributed to genetic factors. n = 1,030
- Including PA (n = 120) and SA (n = 910).

↓

Whole-exome sequencing of DNA from whole blood samples

Gonadal Disorders management of male hypogonadism



DP

At age over 2-2.5 standard deviation(DS) from the population mean
Stage B1 in F, TV < 4 ml in M
Stunted progression for puberty nomograms

Gonadotropin levels

High → Hypergonadotropic hypogonadism

Low

Family hystory of DP
Past medical hystory
New signs/symptoms
Clinical examination

Red flags for organic causes

- ✓Hystory of chronic transfusion regime
- ✓Chronic therapy with Corticosteroids
- ✓Hystory of Chemotherapy /radiotherapy (also possible gonadal failure)
- ✓Others pituitary deficiencies (CPHD)
- ✓Signs/symptoms of impaired thyroid function (hypothyroidism/ hyperthyroidism)
- ✓Signs/symptoms of coeliac disease or Inflammatory bowel disease
- ✓Signs/symptoms of brain mass or infiltrative disorders

Yes → Underlying etiology

No

Red flags for functional HH

Eating disorders
Excessive physical exercise

Yes → Underlying etiology

No → Watchful waiting/ short treatment with sex steroids → Spontaneous resolution

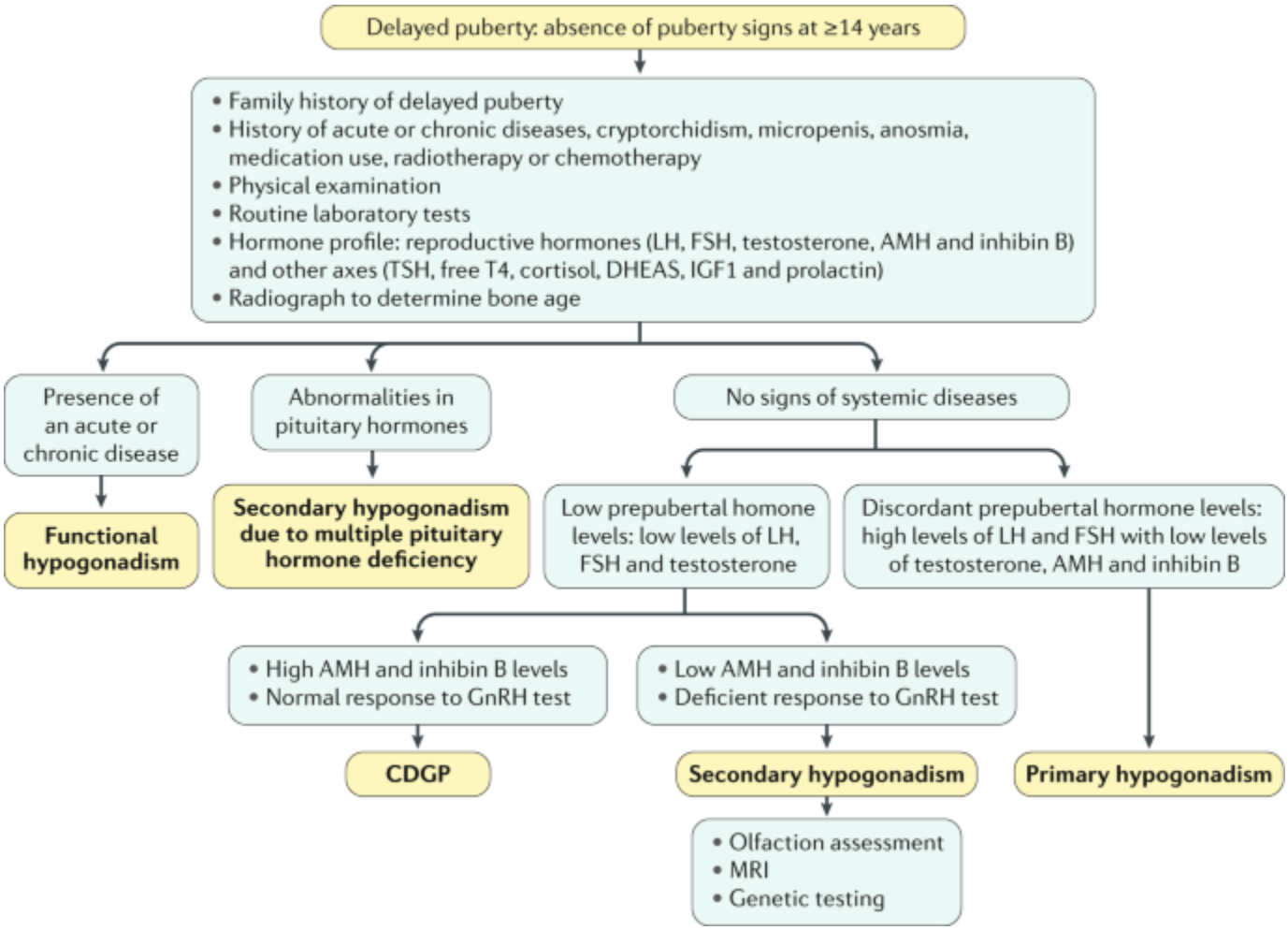
Yes → Self-limited DP

No

Red flags for CHH

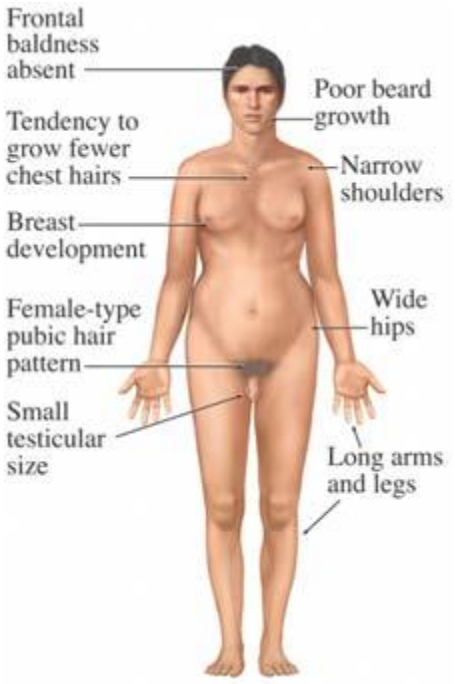
- ✓Micropenis and /or cryptorchidism
- ✓Anosmia/hyposmia
- ✓Deafness
- ✓Cleft lip/palate
- ✓anomalies of hand or foot
- ✓Renal agenesis
- ✓skeletal anomalies
- ✓bimanual synkinesia
- ✓complex malformation (CHARGE syndrome)

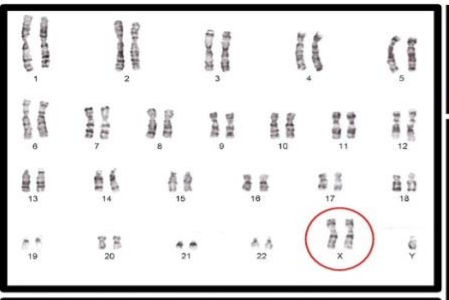
Yes → NGS + Need of Puberty Induction therapy

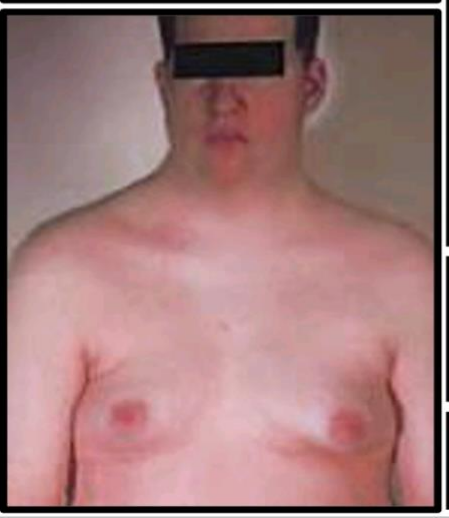

Delayed puberty: absence of puberty signs at ≥14 years
• Family history of delayed puberty
• History of acute or chronic diseases, cryptorchidism, micropenis, anosmia, medication use, radiotherapy or chemotherapy
• Physical examination
• Routine laboratory tests
• Hormone profile: reproductive hormones (LH, FSH, testosterone, AMH and inhibin B) and other axes (TSH, free T4, cortisol, DHEAS, IGF1 and prolactin)
• Radiograph to determine bone age
Presence of an acute or chronic disease
Abnormalities in pituitary hormones
No signs of systemic diseases
Functional hypogonadism
Secondary hypogonadism due to multiple pituitary hormone deficiency
Low prepubertal homone levels: low levels of LH, FSH and testosterone
Discordant prepubertal hormone levels: high levels of LH and FSH with low levels of testosterone, AMH and inhibin B
• High AMH and inhibin B levels
• Normal response to GnRH test
• Low AMH and inhibin B levels
• Deficient response to GnRH test
CDGP
Secondary hypogonadism
Primary hypogonadism
• Olfaction assessment
• MRI
• Genetic testing

KALLMANN SYNDROME

- Kallmann syndrome is a rare (1:50,000 persons) disorder that occurs in familial and sporadic forms.
- 2 most common clinical deficit in the disorder: anosmia and absence of GnRH. Pituitary function is normal.
- The clinical features include anosmia, facial asymmetry, color blindness, renal anomalies, microphallus, and cryptorchidism. The hallmark of the syndrome is a delay in pubertal development.
- Hormone evaluation reveals low testosterone, low LH, and low FSH levels.
- Virilization and fertility can be achieved when given FSH and LH are given to stimulate testis function.







6) Klinefelter Syndrome XXY

❖ Clinical features

Pediatric On Squares

- ✓ **Gynecomastia**
- ✓ Tall stature
- ✓ **Small testes**
- ✓ Micropenis
- ✓ Normal pubic and axillary hair
- ✓ Intellectual disability
- ✓ Infertility
- ✓ Behavioral problems

The most common cause of primary hypogonadism and infertility in males

Recurrence rate 1 – 2 %

❖ Laboratory finding ?

- ✓ Low testosterone
- ✓ High FSH/LH

❖ Increases risk of :

- ✓ Pulmonary disease
- ✓ Varicose vain
- ✓ ADHD

❖ Increases risk of which Malignancies ?

- ✓ Breast cancer
- ✓ Testicular cancer

❖ What is the most effective treatment ?

- ✓ Testosterone replacement therapy

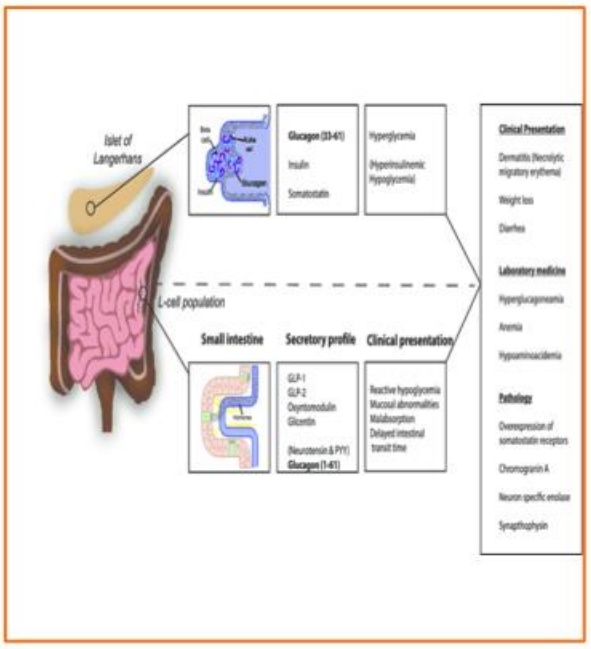
@OnSquares

NDuroEndocrine Tumors

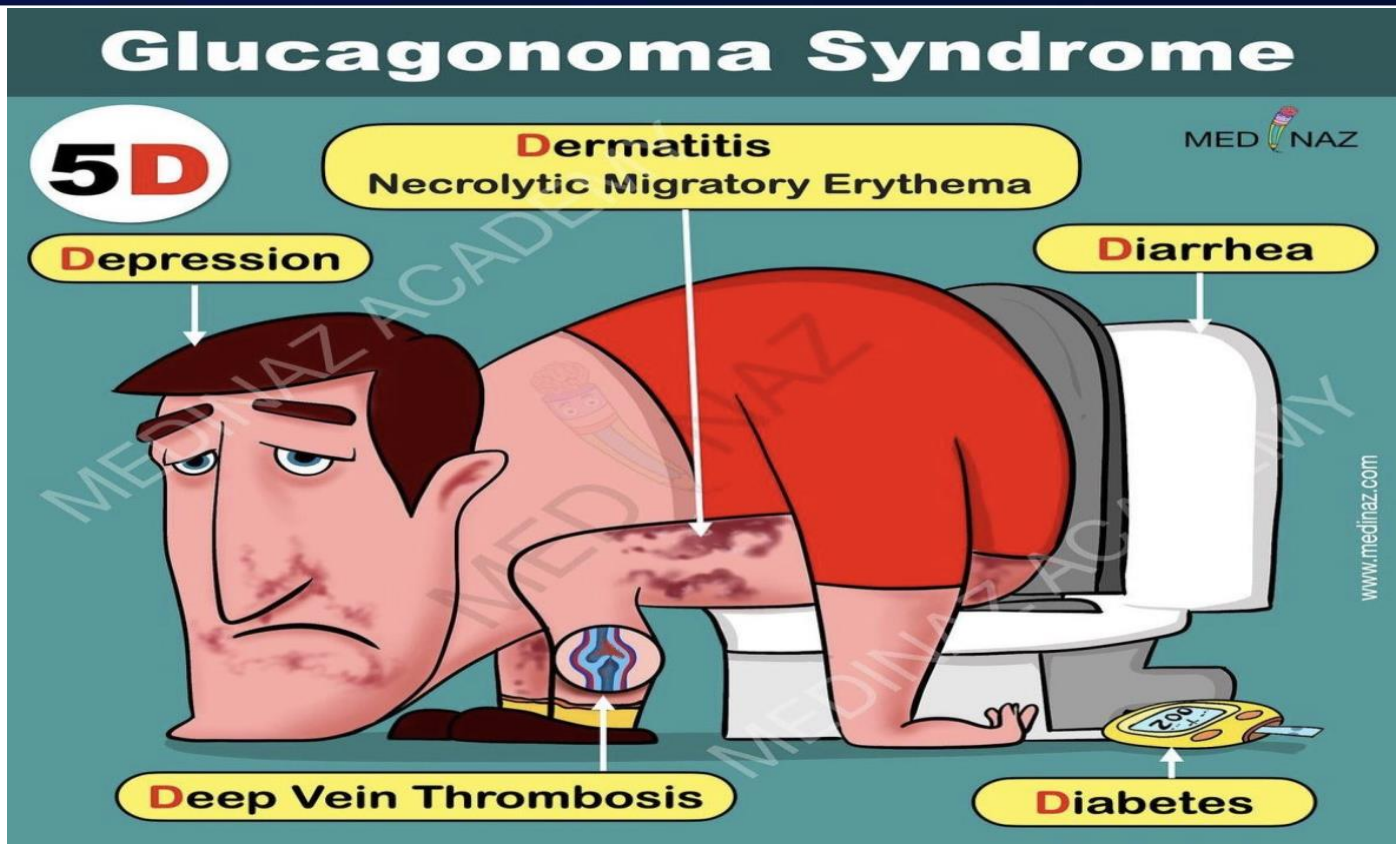
The Glucagonoma Syndrome is caused by a glucagon-secreting pancreatic neuroendocrine neoplasm, #glucagonoma

The syndrome includes: a characteristic rash termed necrolytic migratory erythema, painful glossitis, cheilitis & stomatitis, weight loss, anemia, new-onset or worsening diabetes mellitus, hypo aminoacidemia, low zinc levels, deep vein thrombosis, & depression

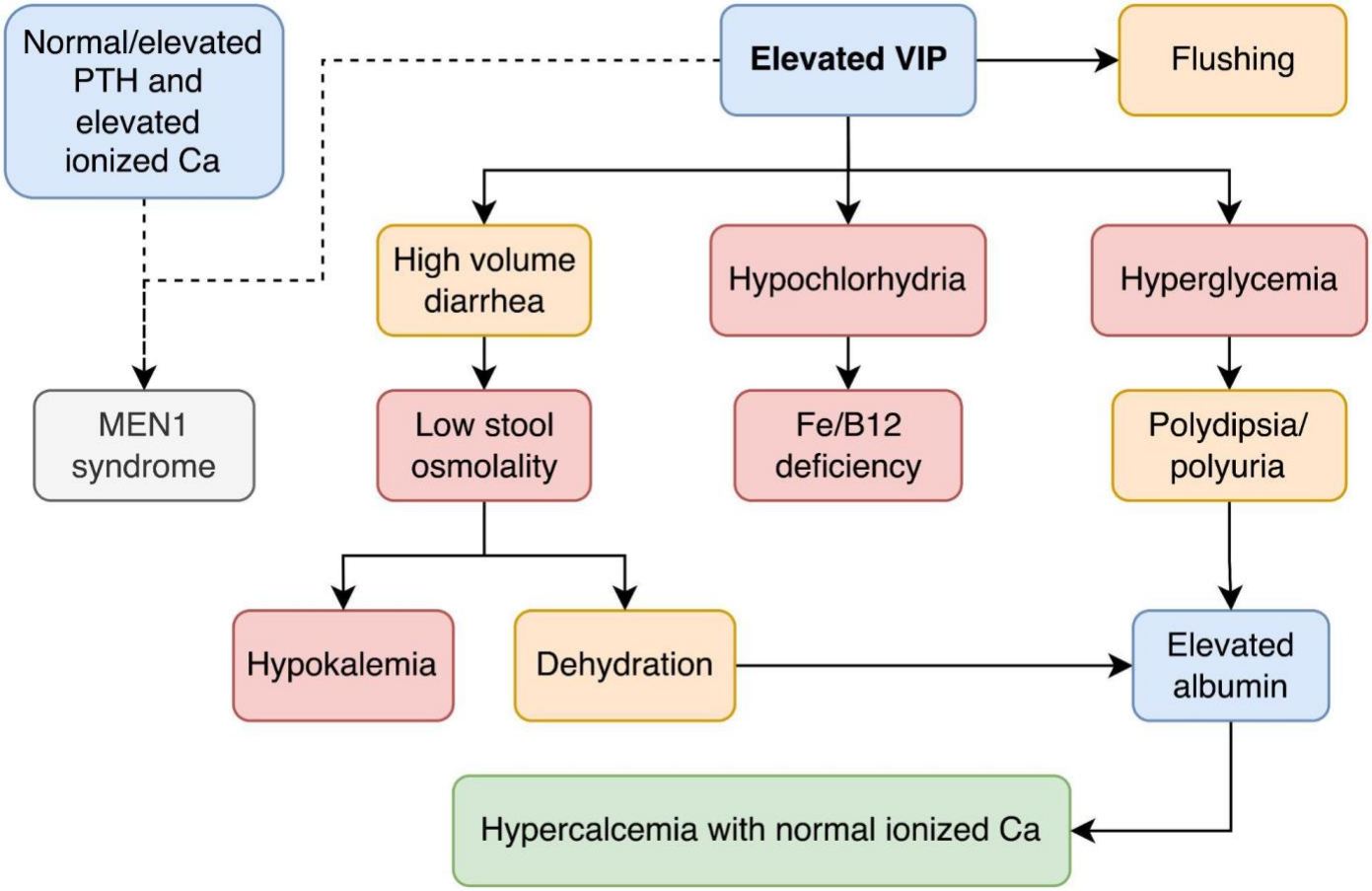
Zandee WT, Hofland J, de Herder WW. Glucagonoma Syndrome. [Updated 2020 Nov 5]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]

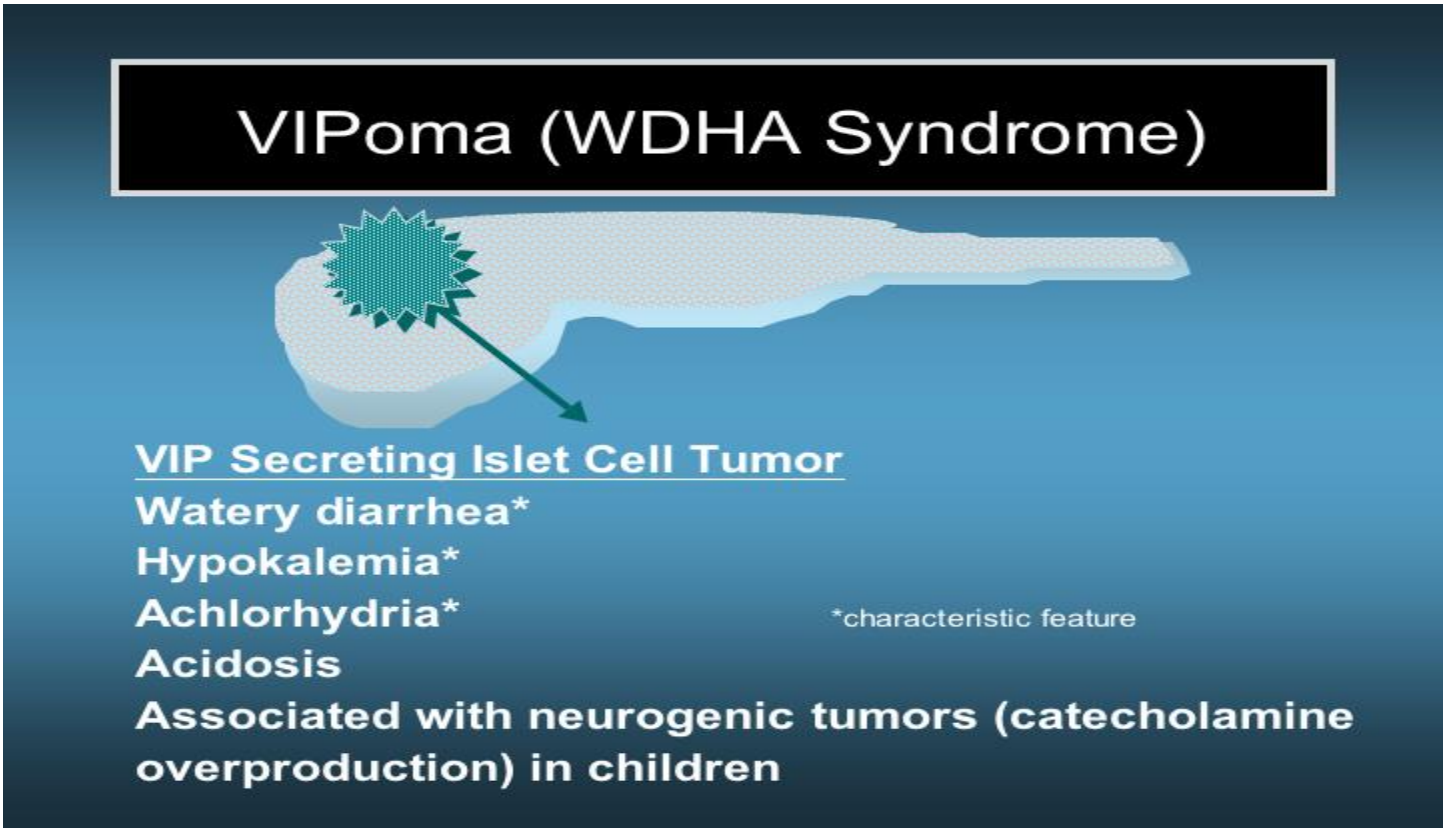


Weweret al., (2016). Do glucagonomas always produce glucagon?. Bosnian Journal of Basic Medical Sciences. 15. 10.17305/bjbms.2015.794.



Vipoma

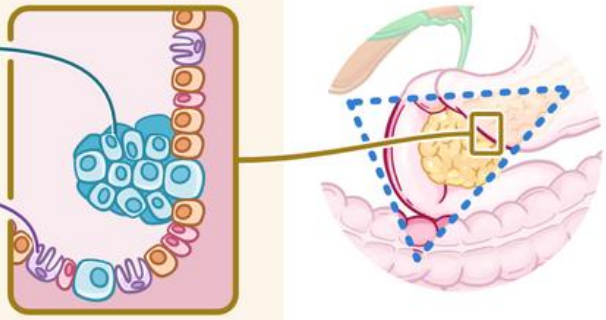

Normal/elevated PTH and elevated ionized Ca
Elevated VIP
Flushing
High volume diarrhea
Hypochlorhydria
Hyperglycemia
MEN1 syndrome
Low stool osmolality
Fe/B12 deficiency
Polydipsia/ polyuria
Hypokalemia
Dehydration
Elevated albumin
Hypercalcemia with normal ionized Ca


VIPoma (WDHA Syndrome)
VIP Secreting Islet Cell Tumor
Watery diarrhea*
Hypokalemia*
Achlorhydria*
Acidosis
*characteristic feature
Associated with neurogenic tumors (catecholamine overproduction) in children

Gastrinoma * Zollinger Ellison syndrome

BACKGROUND

* SMALL NEUROENDOCRINE TUMOR (NET)
* ORIGINATE from **G CELLS**
  - CONTINUOUSLY OVERPRODUCE and RELEASE the HORMONE GASTRIN
  - STIMULATE **PARIETAL CELLS** to SECRETE GASTRIC ACID
  - EXCESS GASTRIC ACID CAN LEAD to EROSION or ULCERS
* MAJORITY LOCATED in the **GASTRIC TRIANGLE**
* CAN BE SOLITARY or DEVELOP in CLUSTERS



SYMPTOMS

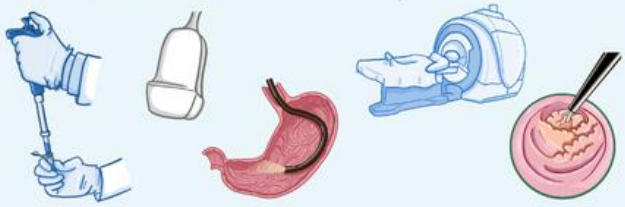
* ASYMPTOMATIC
* ABDOMINAL PAIN
* NAUSEA
* VOMITING
* DIARRHEA
* GASTROESOPHAGEAL REFLUX
* GASTROINTESTINAL BLEEDING
* PEPTIC ULCERS

↓

* **ZOLLINGER-ELLISON SYNDROME**
  - MULTIPLE SEVERE, RECURRENT PEPTIC ULCERS in PART of the SMALL INTESTINE (e.g. duodenum, jejunum)

DIAGNOSIS

* **LABORATORY TESTS:**
  - FASTING SERUM GASTRIN LEVELS
  - SECRETIN STIMULATION TEST
* **IMAGING STUDIES:**
  - ENDOSCOPIC ULTRASOUND
  - DUODENAL ENDOSCOPY
  - ZOLLINGER-ELLISON SYNDROME
    - ~ SOMATOSTATIN RECEPTOR SCINTIGRAPHY
    - ~ COMPUTED TOMOGRAPHY (CT)
    - ~ MAGNETIC RESONANCE IMAGING (MRI)
    - ~ POSITRON EMISSION TOMOGRAPHY (PET)
* **TISSUE BIOPSY**



TREATMENT

* SURGICAL TUMOR REMOVAL
* MEDICATIONS (e.g. proton pump inhibitors, H2 receptor blockers)

OSMOSIS.org

Insulinoma

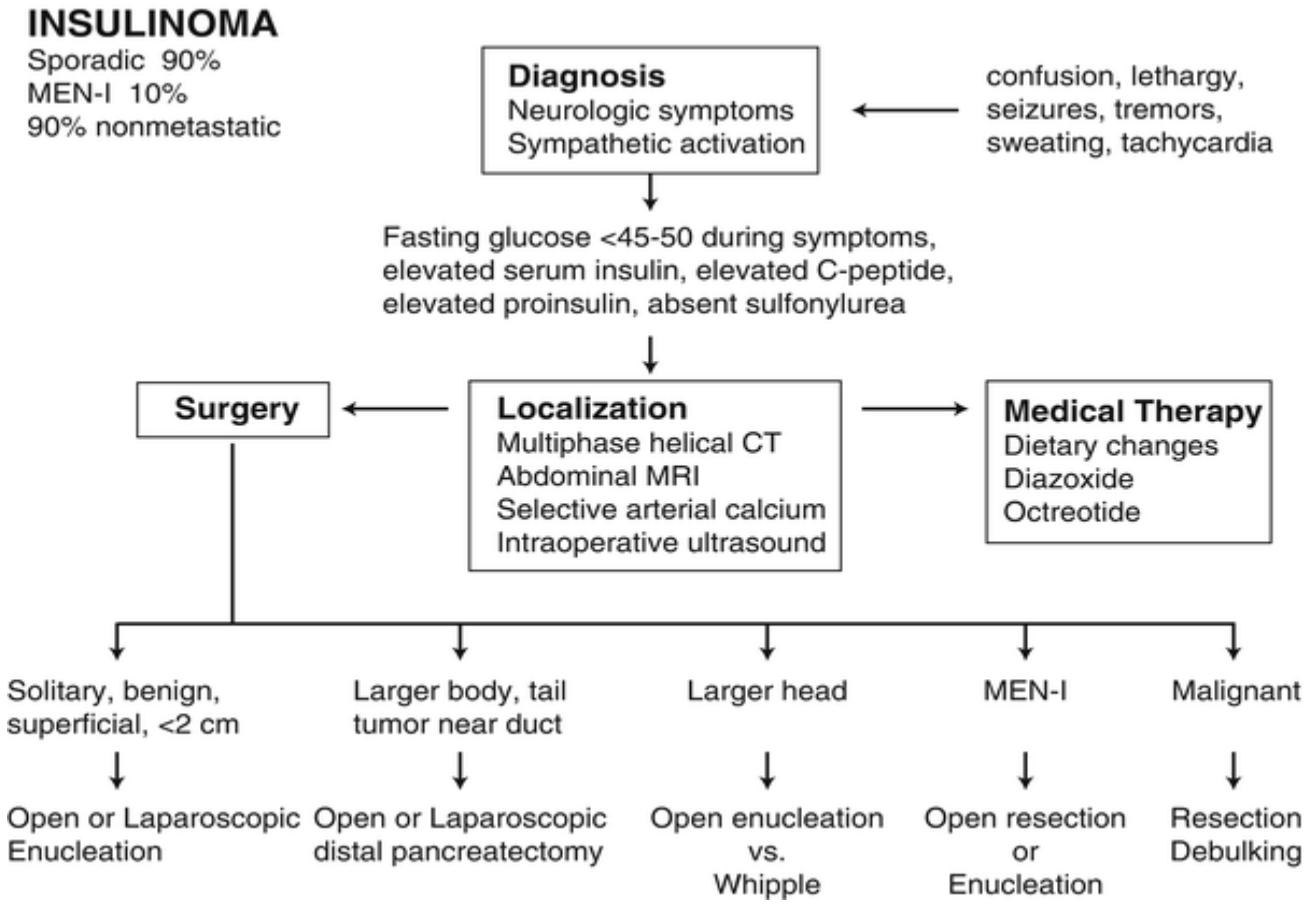
Diagnosis of insulinoma

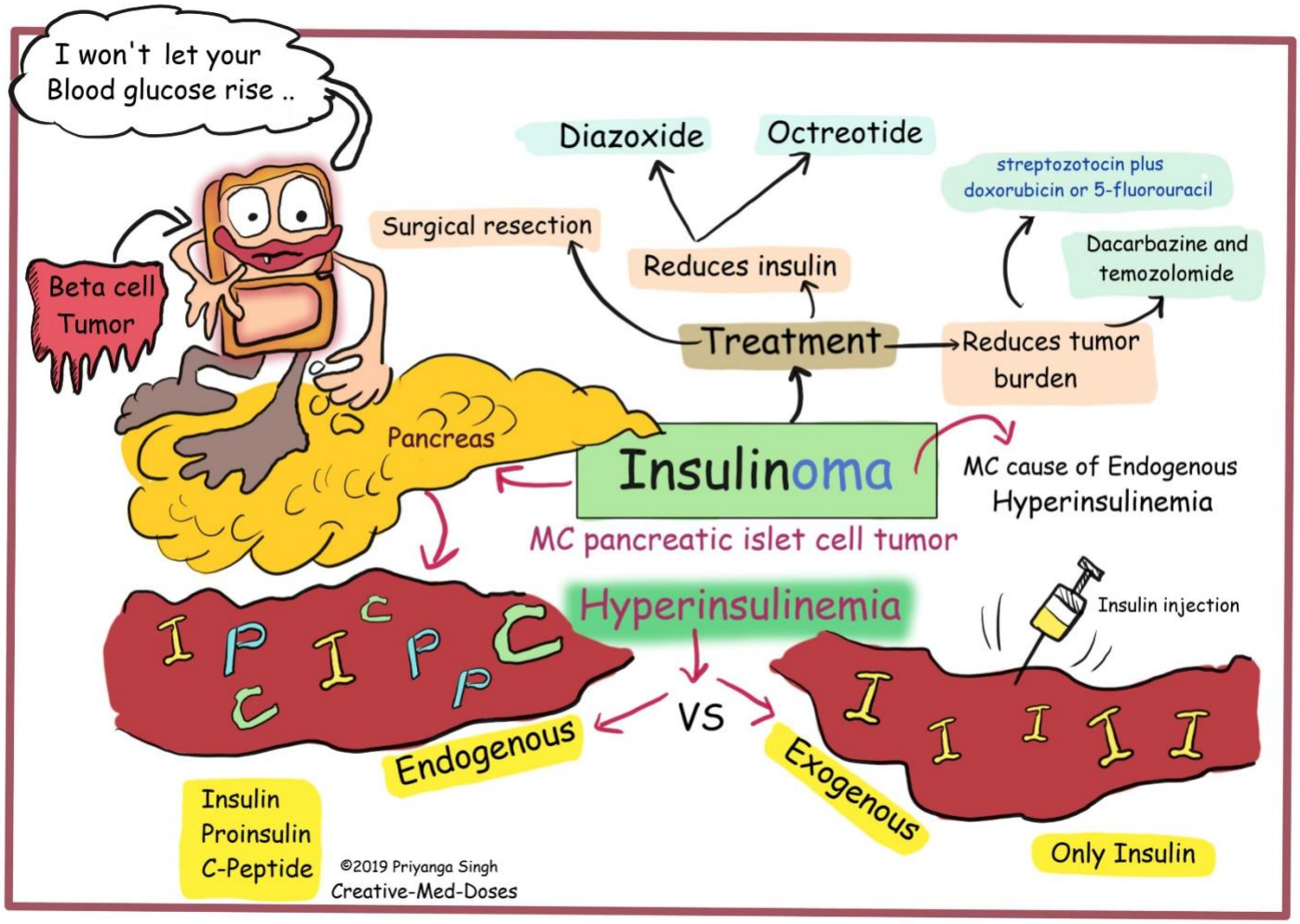
Classical diagnosis

- Hypoglycemia (plasma glucose < 50 mg/dL)
- Neuroglycopenic symptoms
- Prompt relief of symptoms following the administration of glucose

Present consensus

- At the time of hypoglycemia during a 72-h fasting test:
- 5 mIU/L (36 pmol/L) insulin threshold
- 0.6 ng/mL (0.2 nmol/L) C-peptide threshold
- Insulin/C-peptide ratio < 1.0
- 20 pmol/L proinsulin cut-off level
- Absence of sulfonylurea (metabolites) in the plasma or urine





Somatostatinoma

- Usually originate in SI and pancreas
- Syndrome of somatostatinoma
  - Diabetes
  - Gallbladder disease
  - Diarrhea
  - Weight loss
  - Hypochlorhydria
- Rarest of all pNETs

Gout

Etiology: Joint Deposition of Monosodium Urate Crystals

Demographics

♂ > ♀

Middle age—Elderly

Postmenopausal

Dietary Risk Factors

↑ Urate Production

- Obesity
- Increased cell turnover
  - Tumor lysis
  - Hemolytic anemia
  - Myeloproliferative dz
- Lesch–Nyhan syndrome

↓ Urate Excretion

- Diuretics
- Salicylates
- CKD
- Pb toxicity

Acute Gouty Arthritis

Sudden-Onset, Monoarticular

- Erythema
- Tenderness
- Swelling

Commonly involves **1st MTP** (podagra)

Subsides in 10-14 days

Reproduced with permission from Suneja M, Szot JF, LeBlond RF, et al: DeGowin's Diagnostic Examination, 11th ed. New York, NY: McGraw Hill; 2020.

Increased:

- Attack frequency
- # Joints involved

Chronic Gouty Arthritis

Continuous Joint Pain + Acute Attacks

Complications

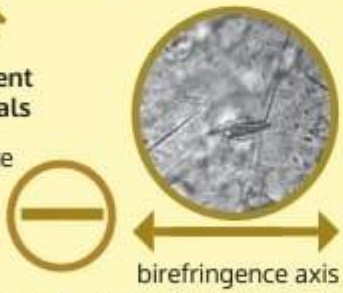
- **Tophi**
- Secondary OA
- Urate kidney stones

(L): Reproduced with permission from Kang S, Amagai M, Bruckner AL, et al: Fitzpatrick's Dermatology, 9th ed. New York, NY: McGraw Hill; 2019.
(R): Reproduced with permission from Sherman SC: Simon's Emergency Orthopedics, 8th ed. New York, NY: McGraw Hill; 2019.

Diagnosis

Arthrocentesis

- **Negatively birefringent needle-shaped crystals**
- Chalky/cloudy aspirate
- 15-20k WBC
- No bacteria



birefringence axis

Serum urate **NOT** helpful for diagnosis

Reproduced with permission from Mitra R: Principles of Rehabilitation Medicine. New York, NY: McGraw Hill; 2019.

Chronic Workup

Joint Radiograph

- "Rat-bite" erosions = chronic disease

24-Hour Urine Urate Excretion

- **If <800 mg,** treat to increase excretion

Reproduced with permission from Elsayes KM, Oldham SA: Introduction to Diagnostic Radiology. New York, NY: McGraw Hill; 2014.

Acute Treatment

Pain Relief + Resolution of Acute Attack

1. **High-dose NSAIDs** (indomethacin, naproxen, ibuprofen)
2. **Colchicine**

if NSAIDs + colchicine ineffective, not tolerated, or contraindicated

3. **Steroids**

Monoarticular → Intra-articular triamcinolone

Polyarticular → PO prednisone

Chronic Treatment

Slow/Prevent Progression to Chronic Gout

1. **Avoid dietary triggers**

Indications for medical therapy: ≥2 Attacks **OR** serum urate >550 **OR** tophi or urate kidney stones

Do **NOT** initiate during acute attack

↓ Urate Production

2. **Xanthine oxidase inhibitors** (allopurinol, febuxostat)

↑ Urate Excretion

2. **Urate reuptake inhibitor** (probenecid)

DR Mina Michae Nesim

References